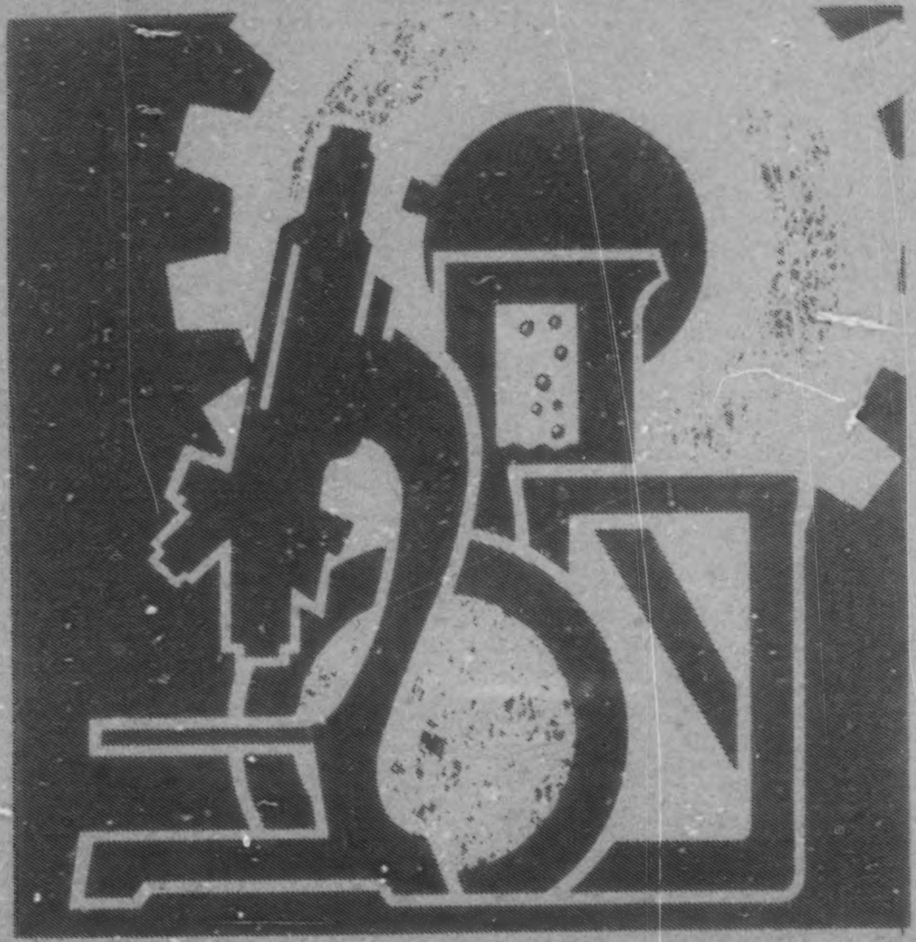
G 76/980

NIOSH GRANTS

NEWARK PUBLIC LIBRARY
APR 21 1981
U. S. GOVT. PUBS.
DEPOSITORY 376

RESEARCH and DEMONSTRATION GRANTS AWARDED in FISCAL YEAR 1980



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
National Institute for Occupational Safety and Health

HE 20.7102:

READEX
FICHE
best copy available

NIOSH GRANTS

1980
RESEARCH AND DEMONSTRATION GRANTS
AND
COOPERATIVE AGREEMENTS
ACTIVE IN FISCAL 1980

PROFESSIONAL MANAGEMENT ASSOCIATES, INC
Silver Spring, Maryland 20910

Contract Number 210-80-0112
February, 1981

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
National Institute for Occupational Safety and Health

April 1981

DISCLAIMER

Mention of company names or products does not constitute endorsement by the National Institute for Occupational Safety and Health.

DHHS (NIOSH) Publication No. 81-117

FOREWORD

The National Institute for Occupational Safety and Health (NIOSH) plans, directs and coordinates research to identify, evaluate and control hazardous working conditions. Under the authorities of the Occupational Safety and Health Act of 1970 and the Federal Mine Safety and Health Act of 1977, NIOSH provides grant support for research and demonstration projects.

This report is published with several purposes in mind. We hope that it will be used as a readily available source of information on the status and scope of the program, and that it will stimulate and encourage an interest in occupational safety and health research among scientists in biomedical, engineering and related disciplines. This report describes objectives, approaches and findings for projects which were active during fiscal year 1980 (October 1, 1979 - September 30, 1980). It includes the announcements which were published to stimulate applications in the areas of occupational dermatology and reproductive hazards in the workplace.

Fiscal year 1980 also was the first time that NIOSH utilized the cooperative agreement as a form of the grant mechanism. Cooperative agreements, which permit ongoing involvement and interaction between NIOSH and the grantee, have been awarded this year to enchance the NIOSH Health Hazard Evaluation program and to support studies on the feasibility of using states to develop a nationwide occupational health surveillance system.

We hope this report reflects the progress which I feel has been made in making the research and demonstration grants program an integral part of occupational safety and health research.

Anthony Robbins

Anthony Robbins, M.D.
Director
National Institute for Occupational
Safety and Health

blank page

TABLE OF CONTENTS

Page

FOREWORD

RESEARCH GRANTS GENERAL PROGRAM ANNOUNCEMENT 1

NIOSH RESEARCH GRANTS APPLICATION FLOW 5

MINING HEALTH PROGRAM ANNOUNCEMENT 7

NIOSH RESEARCH GRANTS BUDGET 15

NIOSH RESEARCH GRANTS COMPONENT AND FUNCTIONS 17

RESEARCH AND DEMONSTRATION GRANT SUMMARIES BY EMPHASIS AREA 19

GRANT DISTRIBUTION BY PROGRAM AREA 211

GRANT DISTRIBUTION BY STATE AND REGION 213

INDEX OF PRINCIPAL INVESTIGATORS 217

INDEX OF GRANTEE INSTITUTIONS 219

CROSS REFERENCE WORDS 221

blank page

NIOSH RESEARCH GRANT PROGRAM ANNOUNCEMENT

National Institute for Occupational Safety and Health

January 2, 1981

PROGRAM ANNOUNCEMENT

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

GRANTS FOR RESEARCH AND DEMONSTRATIONS RELATING TO OCCUPATIONAL SAFETY AND HEALTH

Application receipt dates;

March 1, July 1, and November 1

The National Institute for Occupational Safety and Health (NIOSH) announces that competitive grant applications are being accepted for research and demonstrations relating to occupational safety and health including innovative methods, techniques, and approaches for dealing with occupational safety and health problems.

This support is in the form of project grants not exceeding 5 years.

AUTHORITY

These grants will be awarded and administered by NIOSH under the research and demonstration grant authority of Section 20(a)(1) of the Occupational Safety and Health Act of 1970 (29 U.S.C. 669(a)(1). Program regulations applicable to these grants are contained in Part 87 of Title 42, Code of Federal Regulations, "Research and Demonstration Grants Pertaining to Occupational Safety and Health." Except as otherwise indicated, the basic grant administration policies of the Public Health Service are applicable to this program. Applications responsive to this Program Announcement are not subject to OMB Circular A-95 Clearinghouse and/or Health Systems Agency review.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service Centers for Disease Control
5600 Fishers Lane, Rockville, Maryland 20857

ELIGIBLE APPLICANTS

Eligible applicants may be universities, colleges, research institutions and other public and private nonprofit organizations including State and local governments.

PROGRAM REQUIREMENTS

A research project grant application should be intended and designed to establish, discover, develop, elucidate or confirm information or the underlying mechanisms relating to occupational safety or health, including innovative methods, techniques, and approaches for dealing with occupational safety and health problems.

A demonstration grant application should address, either on a pilot or full-scale basis, the technical or economic feasibility or application of: (1) A new or improved occupational safety or health procedure, method, technique, or system; or (2) an innovative method, technique, or approach for preventing occupational safety or health problems.

Particular emphasis is placed on projects involving the occupational aspects of behavior and neurotoxic effects, cancer, chronic effects of trauma, energy, personal protective equipment, physical agents, reproductive effects, respiratory disease and safety. Additional areas of interest include asbestos and asbestos substitutes, cardiovascular diseases, control technology, digestive diseases, radiation, sidestream smoking, and skin disease.

CRITERIA FOR REVIEW

Applications will be reviewed by an appropriate peer review group on the basis of scientific merit and significance of the project, the competency of the proposed staff in relation to the type of research involved, the feasibility of the project, the likelihood of its producing meaningful results, the proposed project period, and the adequacy of the applicant's resources available for the project and the amount of grant funds necessary for completion.

Demonstration grant applications will be reviewed additionally on the basis of the following criteria:

1. Degree to which project objectives are clearly established, obtainable, and for which progress toward attainment can and will be measured.

2. Availability, adequacy and competence of personnel, facilities, and other resources needed to carry out the project.

3. Degree to which the project can be expected to yield or demonstrate results that will be useful and desirable on a national or regional basis.

4. **Extent of and expected cooperation of industry, unions, or other participants in the project, where applicable.**

In addition a secondary review process will be conducted by NIOSH. Factors considered in this review include:

- **the results of the initial review;**
- **the significance of the proposed research to the published research program of NIOSH.**
- **national needs and program balance, and**
- **policy and budgetary considerations.**

APPLICATION AND AWARD

Applications should be submitted on Form PHS-398 (revised October 1979) or PHS-5161-1 for State and local government applicants. Forms should be available from the institutional business offices or from the addresses listed below. The conventional presentation for grant applications should be utilized and the points identified under Criteria for Review must be fulfilled.

An original and six copies (original and two for State and local governments) of the application should be sent or delivered to:

Application Receipt
Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, Maryland 20205

The name of the applicant institution, principal investigator, and title of the proposed project should be telephoned or mailed to NIOSH at:

Grants Administration and Review Branch, OECSP
National Institute for Occupational Safety and Health
Parklawn Building, Room 8-63
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-4493

The proposed timetable for receiving applications and awarding grants is as follows:

Application Deadline	Primary Review Group Meeting	Secondary Review Meeting	Expected Start Date
March 1	June	Sep	December 1
July 1	Oct/Nov	Jan	April 1
November 1	Feb/Mar	May	July 1

Applications received after the deadline date will be considered with the applications received for the following deadline date.

Awards will be made based on priority score ranking and emphasis area, as well as, availability of funds.

AVAILABILITY OF FUNDS

The Fiscal Year 1981 research grants budget is $5.8 million. Grantees will be expected to cost share a minimum of five percent.

FOR FURTHER INFORMATION CONTACT:

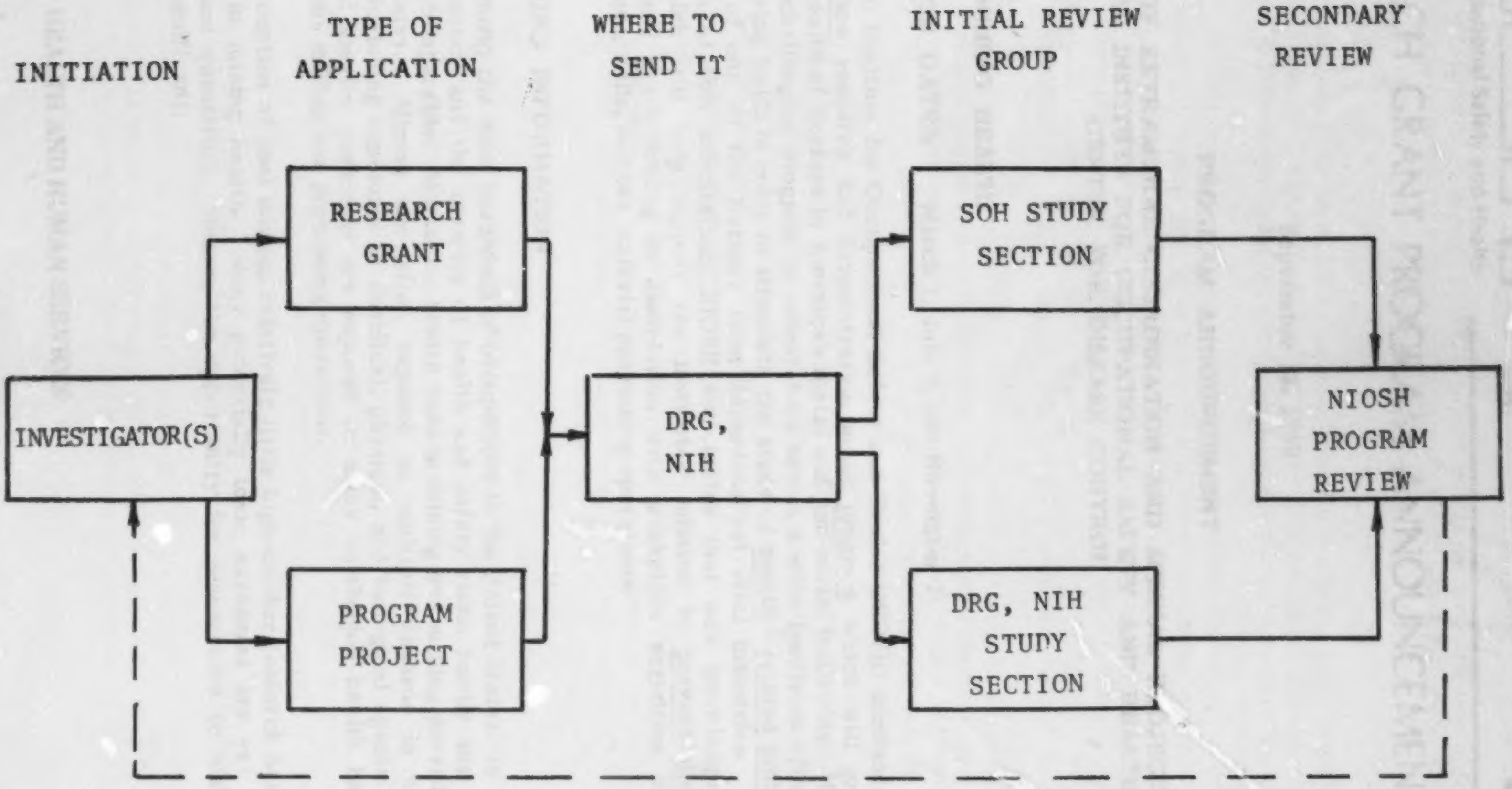
Mr. Joseph W. West
Grants Management Officer, NIOSH
Parklawn Bldg., Room 8-29
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-3122

or

Mr. Roger A. Nelson
Research Grants Program Officer, NIOSH
Parklawn Bldg., Room 8-63
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-4493

(Catalog of Federal Domestic Assistance Program No. 13.262, Occupational Safety and Health Research Grants.)

RESEARCH GRANT APPLICATION FLOW


INITIATION
TYPE OF APPLICATION
WHERE TO SEND IT
INITIAL REVIEW GROUP
SECONDARY REVIEW
INVESTIGATOR(S)
RESEARCH GRANT
PROGRAM PROJECT
DRG, NIH
SOH STUDY SECTION
DRG, NIH STUDY SECTION
NIOSH PROGRAM REVIEW

blank page

NIOSH

National Institute for Occupational Safety and Health

MINING

RESEARCH GRANT PROGRAM ANNOUNCEMENT

September 18, 1980

PROGRAM ANNOUNCEMENT

OFFICE OF EXTRAMURAL COORDINATION AND SPECIAL PROJECTS
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
CENTER FOR DISEASE CONTROL

TITLE: **MINING HEALTH**

APPLICATION DATES: March 1, July 1, and November 1

The National Institute for Occupational Safety and Health (NIOSH) announces an important new research and demonstration grant program which will greatly affect the health of workers in America's metal and non-metal industries. NIOSH offers this challenging program to researchers across a wide spectrum of health and engineering fields in order to stimulate the study of health - related problems and issues of one of the Nation's most hazardous yet vital industries. As a consequence of this solicitation, NIOSH anticipates that new knowledge will emerge which will help support the Institutes' mission to prevent disease, disability, and death arising in association with workplace activities in the Nation's mines, mills, and ore material processing operations.

BACKGROUND INFORMATION

Mining is among the most hazardous of occupations in the United States. In terms of the frequency and the severity of health and safety risks, hardly any other industry is comparable. Moreover, health risks in mining and milling pervade the entire industry. Miners are often exposed to multiple hazards in mining operations including exposures to chemical, physical, and biological agents. Mill workers and service personnel are exposed to many on-the-job health hazards during various milling and processing operations.

With the exception of coal mining, relatively little high-caliber research has been conducted in mining health. Many potentially toxic exposures are yet to be identified and quantified. Hence, the opportunity for researchers to make an impact is significant.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health

High quality mine health research is urgently needed in a number of scientific and technological areas. This Program Announcement identifies some aspects of the present scope of the Institute's interest in the problems of mining-associated occupational diseases.

NIOSH conducts the mine health program set forth in the Federal Mine Safety and Health Amendments Act of 1977 (P.L. 95-164). The Institute is responsible for identifying occupational hazards and for recommending standards and approaches for their control.

Research sponsored by NIOSH offers a means of improving the working conditions and practices in the Nation's coal and metal and non-metal mines and mills in order to prevent occupationally-related disease and death.

RESEARCH GOALS AND SCOPE

The goal of this announcement is to stimulate and encourage high quality grant supported research and demonstration projects in mining health. Study areas are provided below for illustration and direction. Researchers are encouraged to be creative in suggesting new areas of health research.

RESEARCH ENCOMPASSING TRADITIONAL EXTRAMURAL RESEARCH IN LABORATORIES AND CLINICS

- Studies, both epidemiological and clinical, to elucidate the health effects of temperature extremes and pressures, and noise in the mining environment. The health effects of noisy surface operations associated with tipples and preparation plants and the effects of temperature and pressure extremes on ergonomic factors and work practices is also in need of special attention.

- Projects to develop animal models for the study of exposures to substances found in the mining environment, e.g., trace metals, mineral fibers, and radiation.

- Projects to develop methods of detection of pre-clinical cancer in miners.

- Projects which develop analytical methods and application of tests such as sister chromatid exchange and urine analysis of mutagenic agents in exposed miners.

RESEARCH ACTIVITIES IDENTIFYING CAUSAL RELATIONSHIPS

- Projects to monitor pregnancy outcomes including potential teratogenic and perinatal morbidity and mortality effects of women surrounding child-bearing in the mining industry.

- **Studies to document the prevalence of pulmonary disease, especially airway disease, among cohorts exposed to particulates and other pollutants in mining operations and to document the dust levels at which these changes occur.**

- **Epidemiologic studies to determine the incidence and prevalence of various neoplasms which may be associated with exposures during mining, milling, and ore extraction processes.**

- **Studies to identify morbidity and mortality patterns among mine populations related to occupational exposures.**

- **Studies to define the mechanism of action of zeolites, ceramic clays, vermiculite, wollastonite, attapulgite and other naturally occurring mineral fibers in the pathogenesis of disease processes in mammalian systems.**

- **Projects which develop a universal data system for measuring environmental exposure in presently existing mine environments, particularly in high-risk mining exposure environments.**

- **Studies to identify potential carcinogens, mutagens, and teratogens in the mining industry.**

- **Studies which assess the potential interactions between carcinogens and mutagens which may occur at low levels in the mining environment.**

- **Epidemiologic studies, both retrospective and prospective, are needed to determine the long-term multiplicative effects of mining byproducts and radioactive gas exposure on miners and on persons who, although not miners, work with or around the products of mines. Special attention is called to the problem of radon daughters.**

- **Studies to clarify the specific health effects on miners who use explosives in the ore-getting processes and in the coal mining operation processes where the practice of "shot-firing" is used.**

RESEARCH ACTIVITIES ELUCIDATING MECHANISMS FOR PREVENTION

- **Projects to develop surveillance systems which provide for early detection of health impairment and the monitoring of hazardous exposures.**

- **Studies to document the psychological, physiological, and psychosocial impact of shift work on miners.**

- Studies which define specific risk factors including susceptible subpopulations of workers.
- Studies to document the impact of new technologies on the health of workers in mining and milling operations. Particular attention should be given to mineral extraction and benefication technologies and the health effects of diesel exhaust emissions associated with diesel equipment used in underground or closed spaces. The multiplicative effects of diesel emissions, explosives, and other substances such as metals in the mine environment also needs clarification.

RESEARCH PROJECTS DEVELOPING TECHNIQUES AND APPROACHES TO CONTROL ADVERSE HEALTH EFFECTS

- Studies to assess the prevalence of contaminants such as fibrous minerals and metals in mine dust atmospheres.
- Projects are needed which develop sampling strategies and methods for quantifying the exposures that workers are likely to experience in specific job categories in the mining and milling processes in order to allow for the best representation of worker exposure.
- Projects to develop conveniently useful direct-reading measuring devices and personal sampling devices for multiple agents, and devices which would be explosion-proof in the underground mine atmosphere are needed.
- Studies which evaluate successful strategies of control based on specific health parameters.
- Studies which evaluate worker acceptance of protective devices such as respirators and hearing protectors.

REVIEW PROCEDURES AND CRITERIA

The assignment and the arrangement for the initial review of the applications responsive to this Program Announcement will be by the Division of Research Grants. Major factors considered in evaluating each application include:

- training experience, and research competence, or promise, of the applicant(s) to carry out the proposed investigations, and the adequacy of effort (time) to be devoted to the project;
- the scientific merit of the proposal relative to the state-of-the-art of mining health research: the questions proposed for study, the research design, the proposed methodology, the proposed methods for analysis and interpretation of data;

- adequacy and suitability of the existing and proposed facilities and resources;
- appropriateness of the requested budget relative to the work proposed;
- adequacy of collaborative arrangements(s), if applicable.

A secondary review process will be conducted by the Mine Health Research Advisory Committee. Factors considered in this review include:

- the results of the initial review;
- the significance of the proposed research to the research program of NIOSH;
- national needs and program balance; and
- policy and budgetary considerations.

Applications responsive to this Program Announcement are not subject to OMB Circular A-95 Clearinghouse and/or Health Systems Agency review.

Proposals considered to be non-responsive to the terms outlined in this Program Announcement will be appropriately reassigned for review.

MECHANISM OF SUPPORT

The traditional grant-in-aid mechanism will be used to support grants pursuant to this Program Announcement.

Nonprofit organizations and institutions, State and local governments and their agencies, are eligible to apply.

Grants may be supported for up to five years, and may be renewed for an additional period, subject to the competitive review procedure and availability of funds.

Awards will be made based on priority score ranking, as well as availability of funds for this program and program relevance.

Grantees will be required to cost share a minimum of five percent.

Grants will be made under the legislative authorization in Section 501 of the Federal Mine Safety and Health Amendments Act of 1977, Public Law 95-164. The Catalogue of Federal Domestic Assistance Citation is Section 13.262.

METHODS OF APPLYING

Applications should be submitted on PHS Form 398. Applications kits may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Room 448, Westwood Building
Bethesda, Maryland 20205
Telephone: (301) 496-7441

An original and six copies of the application should be sent or delivered to:

Application Receipt
Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
Bethesda, Maryland 20205

The name of the applicant institution, principal investigator, and title of the proposed project should be sent to NIOSH at:

Grants Administration and Review Branch, OECSP
National Institute for Occupational Safety and Health
Parklawn Building, Room 8-63
5600 Fishers Lane
Rockville, Maryland 20857

The proposed timetable for receiving applications and awarding grants is as follows:

Application Deadline	Review Group Meeting Date	Advisory Committee Meeting Date	Expected Start Date
March 1	June	Sep/Oct	December 1
July 1	Oct/Nov	Jan/Feb	April 1
November 1	Feb/Mar	May	July 1

Applications received after the deadline date will be considered with the applications received for the following deadline date.

A brief covering letter should accompany the application indicating that it is submitted in response to this program announcement.

IDENTIFICATION OF CONTACT POINT

Questions related to this announcement should be addressed to:

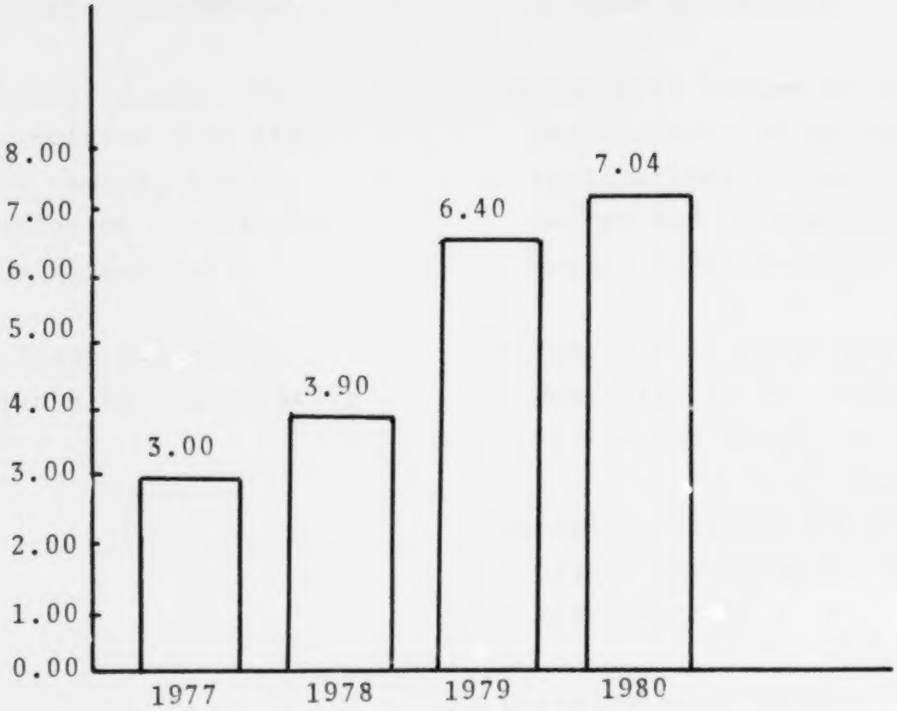
Faye J. Calhoun
Chief, Grants Administrative and
Review Branch, NIOSH
Parklawn Bldg., Room 8-63
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-4493

or

Mr. Joseph W. West
Grants Management Officer, NIOSH
Parklawn Bldg., Room 8-29
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-3122

blank page

NIOSH RESEARCH GRANTS BUDGET
FISCAL YEARS 1977-1980
(millions of dollars)



blank page

RESPONSIBILITIES OF NIOSH GRANT COMPONENTS

GRANTS MANAGEMENT OFFICE (OAMS)

Prepares grant and cooperative agreement award statements

Conducts business management aspects associated with the negotiation, award, and administration of grants and cooperative agreements

Monitors business aspects of awarded grants and cooperative agreements

GRANTS ADMINISTRATION AND REVIEW BRANCH (OECSP)

Contributes to extramural program development

Coordinates review of grant and cooperative agreement applications through the Safety and Occupational Health Study Section

Stimulates research grant applications in institute initiative areas

Monitors progress of awarded grants and cooperative agreements

Coordinates NIOSH grant program with other Agencies and NIH

blank page

RESEARCH AND DEMONSTRATION GRANT SUMMARIES BY EMPHASIS AREA

Emphasis Areas	Page Number
Asbestos and Asbestos Substitutes	21
Behavioral and Neurotoxic Effects	27
Cancer	47
Cardiovascular Diseases	57
Chronic Effects of Trauma	61
Control Technology	69
Dermatology	79
Digestive Diseases	95
Energy	97
Mining	99
Physical Agents	101
Protective Equipment	119
Radiation	125
Reproductive Effects	127
Respiratory Diseases	143
Safety	163
Sidestream Smoking	---
Other Research for Occupational Safety and Health	171

Other NIOSH Grant Programs	Page Number
Demonstrations of Safe Asbestos Removal in Schools	193
Health Hazard Evaluation Cooperative Agreements	205
Surveillance Cooperative Agreements	207

blank page

TITLE: Continuous Optical Monitoring of Asbestos in Air

PROJECT: 5 R01 OH00647-03

PRINCIPAL INVESTIGATOR & ADDRESS: Jan A. Stolwijk, Ph.D.
290 Congress Avenue
New Haven, CT 06519

GRANTEE INSTITUTION: John B. Pierce Foundation Laboratory

OBJECTIVE:

- To develop and test a continuous monitor for the identification and counting of asbestos fibers in the ambient air and in the occupational and residential environment

METHODOLOGY:

An instrument was used that determines the size and asymmetry of dilute suspension of particles largely compared with the wavelength of incident polarized light. The instrument measured the scattering, birefringence or dichroism of the particle as it is aligned, through an external moderate-sized electric field, initially parallel to and subsequently perpendicular to the incident polarized light.

This instrumental technique was based upon theoretical considerations of the behavior of particles in an induced electric field and the ability of a material to become polarized. The determination of these characteristics were translated into particle identification, dimension and their absolute amounts.

PROGRESS & ACCOMPLISHMENTS:

A number of prototypes of the optical fibrous monitor have been tested. In addition, a fluidized bed fiber generator has been built to introduce asbestos fibers into the sampling airstream. The development of hardware and computer programs to detect, differentiate, and quantify the output signals from the prototype asbestos monitor has been completed and will be used in the Health/Schlumberger WH-11 computer.

SIGNIFICANCE TO NIOSH:

Current methods for analyzing asbestos content in the air are difficult and time consuming. The development of an instrument that reliably and quickly monitors asbestos concentrations would greatly assist in the surveying and monitoring process as well as in the implementation of control measures.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date.

PERIOD COVERED: September 15, 1979 - August 31, 1980

TITLE: Shipyard Asbestos Disease: Mortality Experience

PROJECT: 5 R01 OH00682-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Irving Selikoff, M.D.
5th Ave. & 100th Street
New York, NY 10029

GRANTEE INSTITUTION: Mt. Sinai School of Medicine

OBJECTIVES:

- To analyze the mortality experience of a cohort of shipyard workers in order to provide information concerning the extent and nature of asbestos-associated diseases with low-level intermittent episodic exposures
- To develop criteria for a medical surveillance program for current or former shipyard workers

METHODOLOGY:

The cohort for the study consisted of all shipyard workers who were on the rolls of specified unions in February 1967, (approximately 4000 men). Vital statistics including social security number, address, birth date and job classification were available up to 1980. Those who have died were traced from pension records, and the place and date of birth obtained. Subjects were contacted and current status verified. The expected mortality of the entire cohort 1967-1980 was compared to the observed mortality for the same period. The observed mortality was verified by death certificates. Each death was investigated and all available medical data from physicians, hospitals and pathology departments was obtained. Statistical analysis was conducted by key staff.

PROGRESS & ACCOMPLISHMENTS:

Data have been compiled during the year on the mortality experience of all trades personnel employed in the Electric Boat Company's shipyard in Groton, Connecticut for at least 10 years starting on January 31, 1967. Verification of all dates and demographic data has been completed. Statistical analysis of this data is being processed.

SIGNIFICANCE TO NIOSH:

This research provides information on environmental cancer associated with asbestos exposure. The study focuses on the level of risk associated with graduated levels of exposure, taking into account the important variables of duration from onset of exposure and periods of clinical latency.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1979 - May 31, 1980

Asbestos/Cancer/In Vitro/
Toxicology

TITLE: Cocarcinogenic Mechanisms of Asbestos

PROJECT: 1 R01 OH00888-01

PRINCIPAL INVESTIGATOR & ADDRESS:
Brooke T. Mossman, M.D., Ph.D.
Department of Pathology
College of Medicine
Burlington, VT 05405

GRANTEE INSTITUTION: University of Vermont

OBJECTIVES:

- To define the cellular mechanism(s) responsible for the cocarcinogenic effects of chrysotile and crocidolite asbestos in the respiratory tract
- To determine toxic and subtoxic amounts of crocidolite and chrysotile asbestos (alone and in combination with polycyclic hydrocarbons (PCH)) to be used in tracheal organ cultures, grafts and cell cultures
- To document the comparative cellular mechanisms of interactions with both types of asbestos
- To characterize and quantitate the adsorption to and release of the PCH, 3-methylcholanthrine (3MC) from known amounts of asbestos fibers
- To compare the preneoplastic and neoplastic alterations in tracheal grafts and organ cultures exposed to equal amounts (mg per ml medium) of asbestos
- To determine whether or not asbestos acts as a characteristic tumor promoter in the respiratory tract by
    - Stimulation of cellular proliferation
    - Inhibition of differentiation
    - Enhancement of ornithine decarboxylase (ODC) activity
    - Stimulation of plasma membrane associated enzymes
- To obtain sized crocidolite and chrysotile asbestos for studies using tracheal grafts to evaluate the comparative cocarcinogenic effects of long (>10u length) vs. short (< 1 u length) fibers

METHODOLOGY:

This investigation examined the adsorption of benzo (a) pyrene (BP) to acid leached and unleached, sized preparations of both chrysotile and crocidolite asbestos. Leaching alters the surface charge and physical constitution of the fiber. This was accomplished by immersing fiber preparations in 0.1N HCL for varying periods of time. Talc and borosilicate glass fibers were sized and used in comparable studies as examples of particulates with either mineralogical or structural properties similar to asbestos.

The carcinogenic hydrocarbon, BP was coated on the surface of asbestos, talc and borosilicate glass using low temperature precipitation. After coating, the preparations were washed repeatedly with distilled water to remove unbound BP. A radioactive tag of ^{3}H or ^{14}C-BP (New England Nuclear) was incorporated to assess the amounts of BP adsorbed on the fibers using scintillation spectrometry.

Autoradiography was employed to determine the uniformity of the coating of the carcinogen on the fiber surface and, the proportion of the fibers in a given preparation adsorbing the carcinogen. Preparations of BP-treated fibers were dispersed on gelatin-coated slides that were dipped and developed by autoradiographic procedures. Scintillation spectrometry was used to determine the amount of BP bound to a known amount of asbestos, and the binding and release of BP from preparations of asbestos at intervals after precipitation on tracheal organ cultures.

Organ cultures of uniform size will be exposed to BP adsorbed to asbestos and suspended in medium. At 24 hours and at 1, 2, 3 and 4 week intervals, 10 to 12 twelve tissues exposed to each concentration of BP-treated asbestos will be digested using NCS tissue solubilizer and assayed to determine the amount of radiolabeled BP accumulated on (or in) the explant. Data will be analyzed from standard curves of radiolabeled BP using the least square fit of the log technique. The carcinogenicity of BP adsorped asbestos will be compared to effects of BP adsorbed talc and borosilicate glass by implanting treated tracheal organ cultures into syngeneic hamsters. The tumor promoter-like properties of asbestos will be characterized in cell and organ cultures of tracheal epithelium.

PROGRESS & ACCOMPLISHMENTS:

Studies were undertaken to determine the comparative cytotoxicity of chrysotile and crocidolite asbestos in tracheal organ cultures and cell cultures. Chrysotile inhibited cell growth in a dosage dependent fashion at concentrations greater than 1 ug per ml medium. In contrast, crocidolite was more toxic than crocidolite at 10-fold lower concentrations.

In the experimental organ culture system, both chrysotile and crocidolite (at higher concentrations) were cytotoxic to the differentiated superficial cells of the mucosa.

Other results indicate that carcinogenicity is not related absolutely to the amount of 3MC on individual tissues, and that the properties of the minerals which act as carriers of the hydrocarbon are important.

The investigators' results support the findings of epidemiologic studies showing increased numbers of cases of bronchogenic carcinoma in workers exposed to asbestos or hematite.

Other observations suggest that residual asbestos in the lumen of the graft stimulates a brisk immunologic response which may affect loci of developing malignant cells adversely. This is being pursued in other experiments.

Additional studies indicate that stimulation of cellular division and inhibition of differentiation are important mechanisms in asbestos-induced carcinogenesis. Other results suggest that asbestos acts similar to the tumor promoter, 12-0 tetradecanoylphorbol-13-acetate (TPA).

SIGNIFICANCE TO NIOSH:

Although asbestos is a well recognized public health hazard, the mechanism(s) by which it acts to cause respiratory tract neoplastic disease is obscure. This investigation is designed to address this issue, using tools of modern cell biology. Since asbestos is ubiquitous in our environment and human exposure inevitable, an understanding of disease pathogenesis is imperative if appropriate intervention and prophylactic strategies are to be devised.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Mossman, B.T., Craighead, J.E., MacPherson, B.V.:1980: Asbestos-induced Epithelial Changes in Organ Cultures of Hamster Trachea: Inhibition by Retinyl Methyl Ether, Science 207:311-313.

- Mossman, B.T., Halleron, P.A., Craighead, J.E.:1980: Stimulation of Na$^+$-K$^+$ ATPase Activity in Tracheal Epithelial Cells After Exposure to Crocidolite Asbestos, Journal Cell Biology 83:288a.

- Mossman, B.T., Craighead, J.E.:1980: Induction of Tumors in Hamsters After Implantation of Tracheal Organ Cultures Exposed to Crocidolite Asbestos and 3-methylcholanthrene. Proc. American Association Cancer Res. 21:76.

- Craighead, J.E., Mossman, B.T., Bradley, B.J.:1980: Comparative Studies on the Cytotoxicity of Amphibole and Serpentine Asbestos, Environmental Health Perspectives, v. 34, 37-46.

- Mossman, B.T., Adler, K.B., DiCesare, L., Craighead, J.E.: 1980: Interaction of Mineral Dusts with Organ and Cell Cultures Derived from Hamster Tracheal Epithelium. Proc. Int. Workshop on Mineral Dusts *In Vitro*, Pergamon Press.

- Mossman, B.T., Craighead, J.E.:1980: Comparative Cocarcinogenic Effects of Kaolin, Hematite, Carbon and Crocidolite Asbestos in Implanted Hamster Tracheal Organ Cultures. Proc. Fifth International Symposium on Inhaled Particles. Pergamon Press.

- Mossman, B.T., Craighead, J.E.: Mechanisms of Asbestos Carcinogenesis. Environmental Research. In press.

PERIOD COVERED: September 1, 1979 - August 31, 1980

blank page

Behavioral and Neuro/
Clinical/In Vitro/Toxicology/
Animals/Human

TITLE: Neurotoxicity and Teratology of Industrial Chemicals

PROJECT: 5 R01 OH00535-05

PRINIPCAL INVESTIGATOR & ADDRESS:
Peter S. Spencer, Ph.D.
1410 Pelham Parkway
Institute of Neurotoxicology
Bronx, NY 10461

GRANTEE INSTITUTION:
Albert Einstein College
of Medicine

OBJECTIVES:

- To expand our ongoing and productive experimental and clinical studies on the neurotoxic properties of the industrial chemicals acrylamide, and the hexacarbons n-hexone and methyl-n-butyl ketone
- To develop new, sensitive methods for the assessment of chemically induced neurotoxicity and neuroteratogenicity
- To illuminate the mechanism(s) of neurotoxin-induced nerve fiber degeneration
- To study mechanisms of nervous system degeneration following exposure to neurotoxic chemicals used in industry, the capacity of these chemicals for the purposes of determining safe exposure levels, and clinical methods for the early detection of sensory loss in individuals with occupational neurotoxic disease

METHODOLOGY:

Planned studies continued to utilize correlated morphological and biochemical techniques to dissect the mechanisms of axonal degeneration produced by compounds of industrial significance, such as carbon disulfide. Morphological studies investigated the response of the fetal nervous system to common industrial compounds, such as tetralin derivatives. Finally, the modified Optacon^{R}, a simple device for the assessment of decrements in palmar sensation, continued to be tested for its ability to detect sub-clinical occupational neuropathy.

PROGRESS & ACCOMPLISHMENTS

Young adult, male CD-CRL:COBS CD (SD)BR rats were given food *ad libitum* and water containing 2g/1 of Sodium dischloroacetate (DCA), or 0.5% 2,5-hexandedione (2,5-HD), for periods of up to 20 weeks. The brain, spinal cord and peripheral nerves of control and treated animals were examined by light and electron microscopy. 2,5-Hexanedione produced a characteristic pattern of distal, retrograde, giant axonal degeneration in long central and peripheral nerve fibers. In contrast, DCA minimally damaged the peripheral nervous system but, in brain and spinal cord, caused widespread vacuolation of myelin, and dystrophic and degenerative changes in scattered axons. The pattern and distribution of nervous system damage produced by DCA and 2,5-HD appears to be so different that abnormal sterolgenesis seems an unlikely explanation for the pathogenesis of the central-peripheral distal axonopathy produced by neurotoxic gamma diketones.

SIGNIFICANCE TO NIOSH:

The results from this investigation will aid in the development of a screening device to detect subclinical neurological disease in susceptible individuals of the working population. This instrument may prove useful in industrial medicine, since nurses in small factories can be trained to monitor workers who are repeatedly exposed to neurotoxins.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Spencer, P.S., Weinberg, H.J., Krygier-Brevart, V. and Zabrenetzky, V: An in vivo Method to Prepare Normal Schwann Cells Free of Axons and Myeling. Brain Research, in press.
- Schaumburg, H.H. and Spencer, P.S.:1979: Toxic Models of Certain Disorders of the Nervous System - A Teaching Monograph. Neurotoxicology, 1, 209.
- Spencer, P.S. and Schaumburg, H.H: Neurotoxic Chemicals As Probes of Cellular Mechanisms of Neuromuscular Disease. Excerpta Medica, in press.
- Schaumburg, H.H. and Spencer, P.S.:1979: Toxic Models of Disorders of the Peripheral Nervous System. In: Current Topics in Nerve & Muscle Research, North Holland, p. 265.
- Egan, G., Spencer, P.S., Schaumburg, H.H., Murray, K.J., Bischoff, M. and Scala, R.:1980: n-Hexane-"Free" Hexane Misture Fails to Produce Nervous System Damage. Neuropathologica, 1, p. 515-524.
- Krinke, G., Schaumburg, H.H., Spencer, P.S., Thomann, P. and Hess, R.:1979: Clioguinol and 2,5-hexanedione Induce Different Types of Distal Axonopathy in the Dog. Acta Neuropathologica, 47, p. 213.
- Arezzo, J.C. and Schaumburg, H.H.:1980: The Use of the Optacon^R as a Screening Device. A New Technique for Detecting Sensory Loss in Individuals Exposed to Neurotoxins. J. Occup. Med., 22, p. 461.
- Markowitz, L. and Schaumburg, H.H.:1980: Successful Treatment of Inorganic Mercury Neurotoxicity with N-Acetyl-Penicillamine Despite an Adverse Reaction. Neurology, 301, p. 1000.
- Sterman, A.B., Schuaumburg, H.H.::1980: Classification of Neurotoxic Disease by Cellular Target Site. In: Experimental and Clinical Neurotoxicology.
- Spencer, P.S.:1980: Acetyl Ethyl Tetramethyl Tetralin. In: Experimental and Clinical Neurotoxicology, Baltimore, MD, Williams and Wilkins.

- Sabri, M.I., and Spencer, P.S.:1980: Biochemical Mechanisms of Distal Axonopathy. Distal Axonopathies-Biochemical Studies and Hypothetical Mechanisms. In: Experimental and Clinical Neuropathology, Baltimore, MD, Williams and Wilkins.

- Politis, M., Schaumburg, H.H., and Spencer, P.S.:1980: Neurotoxicity of Selected Chemicals. In: Experimental and Clinical Neurotoxicology, Baltimore, MD.

- Spencer, P.S., Bischoff, M.C., and Schaumburg, H.H.:1980: Neuropathology Detection Methods. Neuropathological Methods for the Detection of Neurotoxic Disease. In: Experimental and Clinical Neurotoxicology, Baltimore, MD. Williams and Wilkins.

- Veronesi, B., Peterson, E.R., and Spencer, P.S.:1980: Tissue Culture Model of MnBK Neurotoxicology in Organotypic Tissue Culture. In: Experimental and Clinical Neurotoxicology Baltimore.

- Politis, M.J., Pellegrino, R.G., and Spencer, P.S.:1980: Ultrastructural Studies of the Dying-Back Process. V. Axonal Neurofilaments Accumulate at Sites of 2,5-Hexanedione Application: Evidence for Nerve Fiber Dysfuction in Experimental Hexacarbon Neuropathy. Journal of Neurocytology, 9, p. 505.

- Sterman, A.B., and Schaumburg, H.H.:1980: Neurotoxicity of Selected Drugs. In: Experimental and Clinical Neurotoxicology, Baltimore, MD.

- Spencer, P.S., Schaumburg, H.H., Sabri, M.I., and Veronesi, B.: The Enlarging View of Hexacarbon Neurotoxicity. CRC Critical Reviews in Toxicology, In press.

- Spencer, P.S., Sabri, M.I., and Politis, M.: Methyl n-butyl Ketone, Carbon Disulfide and Acrylamide: Putative Mechanisms of Neurotoxic Damage. In: Progress and Neurotoxicology, Oxford, Pergamon, In press.

PERIOD COVERED: December 1, 1979 - November 30, 1980

TITLE: Repeated Schedule Shifts, Rhythms and Lifespan of Mice

PROJECT: 5 R01 OH00631-03

PRINCIPAL INVESTIGATOR & ADDRESS:	Franz Halberg, M.D. 2642 University Avenue St. Paul, MN 55455
GRANTEE INSTITUTION:	University of Minnesota Medical School

OBJECTIVE:

- To investigate lifespan and circadian rhythms in rodents subjected to repeated shifting of synchronizers (daily lighting and/or feeding schedules).

METHODOLOGY:

This investigation involves systematically examining the effect of repeated shifting of a Light/Darkness (LD) 12:12 lighting regimen upon the lifespan of mice and includes a second synchronizer, meal-timing. The importance of heredity will be assessed by studying two types of mice, first generation hybrid between BALB/c and DEA/2 strains (CDF) and New Zealand Black inbred strain (NZB), throughout their lifespan at various degrees and shifts.

In addition, investigators will examine circadian rhythms under different conditions of study. Selected mice will be implanted with temperature transensors to determine via telemetry the nature and rate of change of temperature rhythms as a result of one or many shifts. Subgroups will be used to examine the possibility of desyn-chronization among circadian rhythms as a result of shifts.

PROGRESS & ACCOMPLISHMENTS:

An automatic feeding system has been developed to control the timing of food accessibility for large numbers of mice. This allows the use of the time of feeding as a second synchronizer of circadian rhythms. The interaction between an LD (12:12) lighting schedule and a feeding schedule will be examined in the context of shifting synchronizers.

SIGNIFICANCE TO NIOSH:

Currently work schedules are empirical and are dictated largely by sociological considerations. Optimization, once it is documented in experimental animals (in physiological terms, i.e., in terms of life duration and quality) may eventually lead to physiological optimization in human beings as well.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Halberg, F.,Powell, E.W., Lubanovic, W., Scheving, L.E., Pasley, P.R., Sothern, E.B. and Broackway, B.:Chronopharmacologic Approach to Vigilance: Models and Methods for Anti-circadian Dyschronic Drug Tests Based on Different Kinds of Murine Thermodyschronism Following Unilateral Or Bilateral Suprachiasmatic Lesion. In press

- Halberg, F., Halberg E. and Halberg, J.:Collateral-Interacting Hierarchy of Rhythm coordination at Different Organization Levels, Changing Schedules and Aging. Pr. Naito Symp. Biorthyum and Its Central Mechanism. In Press. In: Proc. 7th Int. Cong. Pharmacol., Satellite Symp. Pharmacol. and States of Alertness, P. Passouant Ed., Pergamon Press, Oxford. In press

PERIOD COVERED: August 1, 1979 - July 31, 1980

TITLE: Test of Environmental Toxins on Behavior of Mice

PROJECT: 5 R01 OH00706-03

PRINCIPAL INVESTIGATOR & ADDRESS:

Peter B. Dews, M.D.
25 Shattuck Street
Boston, MA 02115

GRANTEE INSTITUTION: Harvard Medical School

OBJECTIVES:

- To develop apparatus and procedures to study schedule-controlled responding as a means of surveying behavioral toxicity of agents
- To develop criteria of behavioral changes that will identify substances causing behavioral chagnes that merit further study

METHODOLOGY:

Mice are trained on a Mult FR 30 FI 300 seconds schedule of reinforcement, then placed in an airtight metal enclosure and exposed to an organic solvent over a range of concentrations. While responding under a mult FR FI schedule of reinforcement to determine dose-behavioral effect curves. The behavioral effects of the exposure are assessed after both acute and chronic exposure.

PROGRESS & ACCOMPLISHMENTS:

A standard procedure for assessing behavioral effects of agents has been established. A dose effect curve for the behavioral effects of toluene and trichloroethylene has been developed.

SIGNIFICANCE TO NIOSH:

A systematic study of the behavioral effects of common industrial solvents on animals may be used to assess the potential effects on humans subjected to similar exposures.

Also, the standardization of a behavioral toxicological method may provide a procedure for the reproducibility of data within and between laboratories.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Wenger, G.R.: 1979: Some Qunatitiative Behavioral Pharmacology in the Mouse, Advances in Behavioral Pharmacology, v. 2. Thompson, T. and Dews, P.B., eds., p. 1-38, New York, Academic Press.

- Dews, P.B. and Wenger, G.R.:1979: Testing for Behavioral Effects of Agents, In Test Methods for Definition of Effects of Toxic Substances on Behavior and Neuromotor Function. Neurobehavioral Toxicology 1: Suppl. 1, p. 119-127.

- Dews, P.B.:1979: Speculations on the Nature of Behavioral Deficits with Aging, In Brain Function in Old Age. Muller, Bayer-Sumposium VII, p. 346-355.

- DeWeese, J. and Dews, P.B.:1979: A Simple Apparatus for Exposing a Mouse to Different Atmospheric Enviornments. Journal of Physiology, 296: pp 6-7.

PERIOD COVERED: May 1, 1979 - April 30, 1980

TITLE: Behavioral and Neurological Effects of Mercury

PROJECT: 2 R01 OH00707-04

PRINCIPAL INVESTIGATOR & ADDRESS:

Gary D. Langolf, Ph.D.
2260 G.G. Brown Laboratory
Ann Arbor, MI 48109

GRANTEE INSTITUTION: University of Michigan

OBJECTIVES:

- To conduct a cross-sectional study of the effects of elemental mercury exposure using recently developed tests of peripheral and central nervous system functions
- To test peripheral nervous system function using electrodiagnostic measurements
- To assess central nervous system function using precision tests of short term memory abilities

METHODOLOGY:

This investigation will test workers exposed to various levels of elemental mercury. The subjects are worker volunteers from two Chlor-alkali plants participating in this on-going three-year longitudinal study. Urinary mercury indices are derived from employees' monthly records.

All electrophysiologic measurements are being performed on the right ulnar nerve.

PROGRESS & ACCOMPLISHMENTS:

One hundred workers have been tested using electrophysiologic and short term memory tests. After the total sample of 150 workers has been tested, cross-sectional statistical analysis will be performed to determine possible effects of mercury exposure in industry.

SIGNIFICANCE TO NIOSH:

This research will determine whether mercury exposure under current industrial conditions is associated with changes in peripheral nerves and short term memory function. If significant associations are found between mercury exposure and test results, investigators will evaluate the threshold of effect in terms of urinary mercury history. This threshold information could be used to re-evaluate current guidelines for exposure control which are based on urinary mercury.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Smith, P.J. and Langolf, G.:1980: The Effects of Mercury Exposure on the Performance of a Binary Classification Task, Proceedings of the Human Factor Society.

PERIOD COVERED: April 1, 1980 - March 31, 1981

TITLE: Occupational Neuropathies Due to Industrial Chemicals

PROJECT: 5 R01 OH00823-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Mohamed B. Abou-Donia, Ph.D.
Dept. of Pharmacology
Durham, NC 27710

GRANTEE INSTITUTION:

Duke University Medical Center

OBJECTIVES:

- To investigate the effect of inhaled hexa-carbon solvents vapors, n-hexane, methyl n-butyl ketone, 2,5 hexandedione and 2,5-hexanediol on the production of delayed neurotoxicity by topically applied o-ethyl 0-4-nitrophenyl phenylphosphonothioate (EPN) which is neurotoxic in hens
- To study the effect of these solvents on hepatic microsomal enzyme activities in hens
- To investigate the effect of hexacarbon solvents on the pharmacokinetics and metabolism of carbon 14-EPN

METHODOLOGY:

Delayed neurotoxicity was induced in 18 month old mature hens by daily application of small doses of EPN. At least five doses of EPN were tested including a "no effect" level. A group of five hens were used for each dose. Two groups of hens were treated (topically) with a daily 10mg/kg dose of tri-o-cresyl phosphate (TOCP) and 10mg/kg of parathion and used as positive and negative controls. A group of untreated hens served as blank controls.

After developing severe signs of neurotoxicity, the hens were anesthetized with sodium barbitone containing heparin, and perfused with 4% sodium paraformaldehyde followed by 5% glutaraldehyde, each in phosphate buffer (PH 7.4). Samples were taken from the sciatic, tibial and peroneal nerves and their branches in the leg, cervical, thoracic and lumber spinal cord, medulla oblongata, optic lobes and other parts of the brain. These tissues were then stained and examined at the light and electron microscopic level.

PROGRESS & ACCOMPLISHMENTS:

Daily dermal administration of EPN (0.01 to 10 mg/kg) on the back of the neck of hens for 90 days produced delayed neurotoxicity. Severity of the clinical condition depended on the size of the daily dermal dose of EPN. Hens given small doses showed only ataxia, while those treated with large doses became paralyzed and died. Days of administration and "total administered dose" before onset of ataxia depended on the daily dose. Degeneration of axons and myelin in the spinal cord was the most consistent histologic change and was identical to that found in TOCP control hens. A group of hens treated daily with a dermal dose of 0.001 mg/kg of EPN remained normal.

Controls consisted of three groups of hens given a daily dermal dose of 20.0 mg/kg of TOCP, 1.0 mg/kg of O,O-diethyl O-4-nitrophenyl phenylphosphorothioate (parathion) in acetone. The third control group was treated daily with an equal dermal dose of acetone. TOCP-treated hens developed delayed neurotoxicity while those given parathion showed inital leg weakness but subsequently recovered without developing delayed neurotoxicity. Controls treated topically with acetone showed no effect. The effect of these treatments on brain acetylcholinesterase and plasma butyrylcholinesterase was investigated. This study showed that subchronic dermal application of EPN was more effective in producing delayed neurotoxicity than subchronic oral administration of the same doses.

SIGNIFICANCE TO NIOSH:

Occupational neuropathy caused by industrial chemicals is a significant problem. The introduction of delayed neurotoxic organophosphorus pesticides as an occupational hazard adds a new dimension to safety considerations of workers. It is expected that the results of this investigation will define the interaction of these chemicals (n-hexane, methy n-butyl ketone, 2,5-hexanedione and 2,5-hexanediol) in terms of their joint clinical biochemical and neuropathological effects.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Abou-Donia, M.B., Graham, D.G., Makkawy, H.M. and Abdo, K.M.: Delayed Neurotoxicity of O-ethyl 0-4-nitrophenyl phenylphosphonothioate (EPN): Subchronic (90 days) Dermal Administration on Hens. Toxicol. Appl. Pharmacol. In press.

PERIOD COVERED: April 1, 1979 - March 31, 1980

TITLE: Occupational Hazards of Acrylamide and Hexane

PROJECT: 1 R01 OH00851-01

PRINCIPAL INVESTIGATOR & ADDRESS:
Peter Spencer, Ph.D.
Neurotoxicology Unit
1410 Pelham Parkway
Bronx, NY 10461

GRANTEE INSTITUTION:
Albert Einstein College
of Medicine

OBJECTIVES:

- To determine the spatial-temporal distribution of distal axonopathy in the brain of adult cats chronically intoxicated with acrylamide and the hexacarbon solvent 2,5-hexanedione
- To determine the relative hierarchy of vulnerability of the cat brain, spinal cord and peripheral nervous system (PNS) in acrylamide and hexacarbon intoxication
- To determine the ability of the feline central nervous system (CNS) and PNS to recover from distal axonopathy
- To examine and compare the effects of acute and chronic acrylamide and chronic 2,5-hexanedione intoxication on the fetal, post-natal, adult and aged rat nervous system
- To examine the fetal and post-natal brain for abnormalities of development produced by chronic, maternal intoxication with acrylamide and 2,5-hexanedione
- To examine the effects of acrylamide and hexacarbon compounds on the Schwann cell, oligodendrocyte and astrocyte
- To research the use of the Biothesiometer^R, Optacon^R and EMG in developing a reliable, rapid, quantifiable means of detecting sub-clinical neuropathy among workers exposed to acrylamide and n-hexane

METHODOLOGY:

Spatial-Temporal Distribution of Brain Damage. A total of 10 cats will be used for this study, five for acrylamide and five for 2,5-hexanedione. Animals will be intoxicated for 30, 60, 120, 180 and 360 days with 10mg/kg/day of acrylamide, or 300 mg/kg/day of 2,5-hexanedione, administered in the drinking water. The clinical course of intoxicated animals will be followed. Weight charts will be constructed and food and water intake monitored. One animal will be anesthetized and perfused with fixatives at each timepoint and standard tissues from the CNS will be taken and prepared for light and electron microscopy.

Tissue will be sampled and immersed in Dalton's chrome osmium tetroxide for one hour of postfixation. After alcohol dehydration, upon infiltration, block hardening and trimming, one micrometer section will be cut with a glass knife in a Proter Blum Mt2B, mounted on glass slides and stained with a 1% aquerous solution of toluidine blue with 0.5% borax for 1 minute at 300°C. These will be examined with a light microscope. Areas will be selected for ultrastructural study, the block trimmed appropriately, and thin sections cut with a diamond knife mounted in an ultramicrotome. Thin sections, collected on copper grids, will be stained with an alcoholic solution of uranyl acetate followed by an aqueous solution of lead citrate, washed, carbon coated, and examined in an electron microscope.

PROGRESS & ACCOMPLISHMENTS:

Accomplishments will be reported at the end of this project period.

SIGNIFICANCE TO NIOSH:

The results of this research may be applicable to employee health testing.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: May 1, 1980 - April 30, 1981

TITLE: Sleep of Shift Workers

PROJECT: 2 R01 OH00917-03

PRINCIPAL INVESTIGATOR & ADDRESS:

Donald I. Tepas, Ph.D.
Department of Psychology
IIT Center
Chicago, IL 60616

GRANTEE INSTITUTION: Illinois Institute of Technology

OBJECTIVES:

- To examine the effects of shiftwork on sleep and related behavior

METHODOLOGY:

This investigation combines survey, clinical, laboratory and interview methods. Electroencephalogram sleep stages, involved in brain response, body temperature, urine volume, mood, and performance were measured in the laboratory on a sample worker population. Standardized evaluation instruments were used to assess the personality, job satisfaction, medical history, adjustment, and mood states of the men and women participating in the study. Interview data concerning the sleep, health, adjustment, home and community life of these workers were collected. The sleep-related influence of job duties, work shift and work shift experience is being examined.

PROGRESS & ACCOMPLISHMENTS:

Surveys have been administered to 1500 workers in the Chicago and St. Louis area. Over 100 workers have been studied in the laboratory and 80 workers have been given extensive interviews. A detailed analysis of the data is in progress. The data indicate that night shift workers manifest significantly decreased sleep periods and decrements in performance on standardized laboratory tests. Preliminary data indicate significant differences in their home and community life.

SIGNIFICANCE TO NIOSH:

Currently, little data is available on shift work among U.S. workers as it relates to sleep. The results of this study may provide new quantitative information on how shift work is related to sleep as well as the general health and safety of working men and women.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Tepas, D.I., Maltese, J.W., Stock, C.G. and Walsh, J.K.:1979: Sleep Habits of Workers Reporting High and Low Drug Use. Electroencephalography and Clinical Neurophysiology, 46, No. 5, p. 32.

- Walsh, J.K.: 1979: Evoked Brain Responses to Auditory and Visual Stimuli of Equal Subjective Magnitude. Perception and Psychophysics, 26, p. 396-402.
- Browman, C.P.:1979: Diurnal Variation of Human Auditory Evoked Potential. Physiological Psychology, 7, p. 287-390.
- Tepas, D.I.:1979: Methodological Approaches to the Study of Shift Work, Behavior Research Methods and Instrumentation, 11, p. 3-4.
- Gordon, G.C., Tepas, D.I. Stock, C.G. and Walsh, J.K.:1979: Gaining Access to Shift Workers Through Labor Unions, Behavior Research Methods and Instrumentation, 11, p. 14-17.
- Walsh, J.K., Gordon, G.C., Maltese, J.W., McGill, W.L., and Tepas, D.I.:1979: Laboratory and Field Interview Methods for the Study of Shift Workers, Behavior Research Methods and Instrumentation, 11, p.18-23.
- Walsh, J.K., Tepas, D.I., and Dolgin, D.L.:1979: The EEG Sleep of Chronic Night Workers: Preliminary Findings. Sleep Research, 8, p. 288.
- Browman, C.P., and Sullivan, H.T.:1980: Human Auditory Evoked Potentials: Reliability of Intensity Functions, 5, p. 207-210.

PERIOD COVERED: November 1, 1979 - October 31, 1980

TITLE: Chronobiology and Occupational Health Hazards

PROJECT: 1 R01 OH00952-01

PRINICIPAL INVESTIGATOR & ADDRESS: Lawrence Scheving, Ph.D.
Department of Anatomy
4301 West Markham
Little Rock, AR 72201

GRANTEE INSTITUTION: University of Arkansas

OBJECTIVES:

- To test the role of rhythms in influencing the outcome of toxicity tests
- To examine carcinogens, from the viewpoint of circadian-stage dependence, under a variety of conditions compatible with the usual working day of the laboratory
- To explore rhythms in temperature and other selected variables to see if they can be used as sensitive gauges or serve as harbingers of early pathology

METHODOLOGY:

In this investigation, agents-malathion, paraquat, ethyl carbonate and mercuric chloride were given at six time points in four hour intervals over a 24 hour span to separate subgroups of animals standardized in isolation chambers. The regimen consisted of eight hours of light alternating with sixteen hours of darkness (LD 8:16). Five dosages bracketing the lethal dose (LD50) range were used at each time point. Death of the animals will be the end point studied.

It was expected that the degree of toxicity as expressed by the mortality in each group would vary as a function of the time the mice were injected. The results from the first step in the investigation should serve as the selection of one of the four agents and of an "optional" dosage to be employed throughout this investigation.

PROGRESS & ACCOMPLISHMENTS:

Research has concentrated on two different light/dark schedules on their ability to phase-shift several rhythmic variables, in order to select the one that could make chronobiology practical, in that experiments could be carried out within the confines of a normal working day.

Among the rhythmic variables most extensively studied to date are DNA synthesis in the esophagus, rectum, spleen and bone marrow, and the mitotic index of the corneal epithelium. Findings indicate that it takes three weeks to invert all of the above rhythms, although a number of them can be inverted within one week.

Investigators have also studied the effect of staggered light/dark schedules on these same rhythms and conclude that this technique of synchronizing also takes 21 days to phase-shift all of the above rhythms. In addition, a number of studies have been done demonstrating dramatic variation in susceptibility to x-radiation. For example, variation in toxicity as measured by percent survivors ranged from 26.8% to 92.9%. The animals were least resistant to irradiation during mid-light.

SIGNIFICANCE TO NIOSH:

The results from this investigation should document in mice the circadian susceptibility cycles for the acute toxicity of four compounds which may play a role in occupational and environmental toxicology.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: December 1, 1979 - November 30, 1980

TITLE: New Behavioral Tests for Occupational Solvent Risks

PROJECT: 1 R01 OH00973-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Hugh L. Evans, Ph.D.
550 First Avenue
New York, NY 10016

GRANTEE INSTITUTION: New York University Medical Center

OBJECTIVE:

- To demonstrate the utility of new assays for neurotoxicity induced by organic solvents

METHODOLOGY:

Mice, pigeons, and monkeys will be the animal models used in this study to determine appetitie changes and sleep disturbances which result from sub-chronic inhalation of either toluene, trichoroethylene(TCE) or n-hexane. Locomotor activitiy as well as CO_2 production will be measured. Behavioral, metabolic, and histopathologic changes will be determined.

Established dynamic vapor generation techniques will be used. The inhalation exposures will be controlled by use of standard analytical techniques. Samples will be drawn through charcoal tubes, desorbed into carbon disulfide and analyzed with a gas chromatograph equipped with a flame-ionization detector.

PROGRESS & ACCOMPLISHMENTS:

This is a new grant. Progress and accomplishments will be reported in the FY 81 grant report.

SIGNIFICANCE TO NIOSH:

It is expected that this study will relate the consequences of low level exposure of organic solvents to important behavioral functions, and provide new animal models for human symptoms that result from solvent inhalation.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date.

PERIOD COVERED: August 1, 1980 - July 31, 1981

Behavioral and Neuro
Clinical Study/In Vivo

TITLE: Neurotoxic Assessment of Occupational Exposure to Lead: Electrophysiologic/Psychologic Aspects

PROJECT: 1 R01 OH00984-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Robert G. Feldman, M.D.
75 East Newton Street
Boston, MA 02118

GRANTEE INSTITUTION:

Boston University
University Hospital

OBJECTIVES:

- To identify the most sensitive, specific and reproducible screening methods for detecting disturbed central and peripheral nervous system function in workers exposed to lead
- To develop a standard protocol for the performance of electro-diagnostic and psychologic testing, to establish criteria for evaluating test reliability and to simplify such a protocol so that it might be employed reliably by a properly trained technician

METHODOLOGY:

A group of 40 workers occupationally exposed to lead (history of occupational lead exposure of at least one year) and a control group of 40 workers from the same age range and similar educational level, but without exposure to lead during the last year, will be studied and restudied one and three years later. One week after the initial testing, 30 percent of the subjects will be retested to check the reproducibility of the methods. The procedures will include:

- A questionnaire concerning background information and subjective symptoms
- Nerve conduction velocity in the motor and sensory fibers of the ulnar nerve, motor conduction velocity of the sural nerve on one side of the body as well as amplitude measurements of the motor action potentials
- Clinical neurological examination
- Psychological evaluation including memory tests, tests of overall intelligence, test on sustained attention, tests on dexterity and eye-hand coordination, and a self report scale for measuring mood state
- Biological monitoring data: bi-monthly measurements of blood lead zinc protoporphyrin

PROGRESS & ACCOMPLISHMENTS:

At the Plant, 108 subjects have been enrolled. All data have been collected and is currently being analyzed.

It has been determined that one of the psychological tests has a definite positive correlation to and is very sensitive to lead exposure.

SIGNIFICANCE TO NIOSH:

This study should provide the basis for developing recommendations of peripheral and nervous system tests to be used in the examination of workers exposed to known or suspected neurotoxins. The results from this study should broaden the knowledge and understanding of the effects of lead on the nervous system.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: April 1, 1980 - March 31, 1981

Cancer/In Vivo/Animals/
Toxicology

TITLE: Mechanism of Action: Carcinogenic C-Methylarylamines

PROJECT: 5 R01 OH00611-05

PRINCIPAL INVESTIGATOR & ADDRESS:

John H. Weisbuger, Ph.D.
Dana Road
Valhalla, NY 10595

GRANTEE INSTITUTION: American Health Foundation

OBJECTIVES:

- To elucidate the metabolism and mechanism of action of the carcinogen 2 - amino-3-methylnophthalane (AMN) and 3,2 di-methyl-4-aminobiphenyl (DMAP)
- To synthetize DMAP specifically labelled with 14 in 3- methyl position
- To identify the metabolites of DMAP in the bile and urine of rats and hamsters in order to account for possible differences in carcinogenicity

METHODOLOGY:

This procedure involves the clarification of the activation and detoxication pathways in vivo using Carbon-14 labeled carcinogens. To test the working hypothesis that the o-methylamino effect involves oxidation of the methyl group, another approach involves the synthesis of derivatives in which the amino group and the o-methyl group are progressively in mutagenicity oxidized with derivatives devoid of the o-methyl group, assays and when indicated, in rats, hamsters and mice for carcinogenicity.

PROGRESS & ACCOMPLISHMENTS:

In conformity with the fact that these compounds caused bladder cancer in hamsters, but colon cancer in rats, it was found that more metabolites were expected in the urine of hamsters than in rats, but in bile the reverse was true.

SIGNIFICANCE TO NIOSH:

It is expected that these studies will lead to an understanding of certain facets of carcinogenesis by 3-methyl-2-naphthylamine and DMAP as well as to an overall understanding of their modes of action. This is particularly important in view of the widespread use of these and related compounds in cancer induction. An insight into the metabolic pathways and interaction of these chemicals will assist in elucidating the mechanism of action and may provide leads for rational preventive measures.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Hecht, S.S., El-Bayoumy, K., Tulley, L., and LaVoie, E.:1979: Structure-Mutagenicity Relationships of N-Oxidized Derivations of aniline, o-Toluidine, 2'-Methyl-4-aminobiphenyl, and 3,4'-Dimethyl-4-aminobiphenyl. J. of Medicinal Chem., 22:8, 981.
- Williams, G.M., Chandrasekaran V., and Weisburger, J.H.: The Carcinogenicity of 3-Methyl-2-naphthylamine and 3,2'Dimethyl-4-aminobiphenyl to the Bladder in Syrian Golden Hamsters. In press.
- Williams, G.M., Chandrasekaran, V., and Weisburger, J.H.: The Carconogenicity of 3,2'Dimethyl-4-aminobiphenyl for the Gastro-intestinal Tract of Syrian Golden Hamster with Atypical Proliferative Enteritis and the Effect of Disulfiram. In press.

PERIOD COVERED: December 1, 1979 - November 30, 1980

Cancer/Physical Agents/
Epidemiology/In Vivo/
Human/Toxicology

TITLE: Cohort Mortality Study of Dimethylnitrosamine Workers

PROJECT 5 R01 OH00690-03

PRINCIPAL INVESTIGATOR & ADDRESS:

William Nicholson, Ph.D.
1 Gustave Levy Place
New York, NY 10029

GRANTEE INSTITUTION:

Mt. Sinai School of
Medicine - CUNY

OBJECTIVE:

- To assess the potential human carcinogenicity of exposure to dimethylnitrosamine and other nitrosamines

METHODOLOGY:

Employment rosters and union records were used for the identification of the cohort. The tracing of the members of the cohort has been done. The full mortality experience of the cohort is being studied and observed rates of death by cause have been tabulated in search for unusual mortality patterns. Cause of death will be calculated using appropriate age, sex, race, calendar period, and location specific data from the National Office of Vital Statistics on a person years-at-risk basis. The calculated rates will be compared with those observed at yearly intervals during the course of this research. The individuals in the study will be characterized according to exposure categories defined by company environmental measurements, by the data from periodic blood analysis for SGOT and SGPT, and by descriptions of work activities and circumstances.

PROGRESS & ACCOMPLISHMENTS:

Initial tracing of a cohort of 348 workers exposed to dimethylnitrosamine has been accomplished with all but twenty individuals located with vital status determined. While forty-five deaths have occurred, this number is too small for meaningful analysis. A second cohort of 1,120 workers potentially exposed to nitrosamines in a ball-bearing manufacturing plant have also been identified and traced. The nitrosamine exposures here would result from the use of synthetic cutting oils in which diethanolnitrosamine could have formed through the interaction of nitrite rust inhibitors with the components of the synthetic oil. The preliminary results of this latter group suggest the presence of excess cancer, particularly of the kidney. Further follow-up of each group is continuing.

SIGNIFICANCE TO NIOSH:

This study will assess the possible long term effects of dimethylnitrosamine in an established cohort of workers.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1979 - July 31, 1980

TITLE: Cancer Risks in Cosmetologists

PROJECT: 5 R01 OH00780-02

PRINCIPAL INVESTIGATOR & ADDRESS:

J. Wister Meigs, M.D.
Connecticut Cancer
Epidemiology Unit
60 College Street
New Haven, CT 06510

GRANTEE INSTITUTION:

Yale University School
of Medicine

OBJECTIVES:

- To investigate the incidence of cancer of all sites among cosmetologists who were licensed in Connecticut before December 1965
- To obtain a more definitive test of preliminary results which suggest that the cosmetologists have an increased risk of getting acute leukemia
- To increase the size of the study group by including in the target population 5,000 cosmetologists whose dates of birth were previously unavailable

METHODOLOGY:

The target population includes all cosmetologists, who were registered in Connecticut and who began hairdressing school before December 31, 1965. The cosmetologists are divided into five license categories which include instructor, registered hairdressers, assistant hairdressers, operators and manicurists.

Two groups are being used as comparison groups for the cosmetologists: the population of the state of Connecticut with Tumor Registry computed incidence rates and, Connecticut school teachers who will be individually matched to the cosmetologists.

PROGRESS & ACCOMPLISHMENTS:

Information in addition to that contained in the records has been obtained from approximately 3,500 cosmetologists and vital status has been updated through 1978 for the entire cohort. Computerized linkage has been completed on the names of the Connecticut tumor registry with those of the cohort.

SIGNIFICANCE TO NIOSH:

This project may contribute a procedure for the study of as well as incidence rate of cancer among cosmetolgists.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 1, 1979 - August 31, 1980

TITLE: Lung Cancer Screening of Workers at High Risk

PROJECT: 1 R01 OH00914-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Charles Mittman, M.D.
1500 E. Durate Road
Durate, CA 91010

GRANTEE INSTITUTION: City of Hope Medical Center

OBJECTIVES:

- To determine if strategies can be developed to predict and/or prevent lung cancers in steel workers exposed to the coke oven environment known to increase the cancer risk
- To evaluate the effectiveness for the early detection of lung cancer by estimating the sensitivity and specificity of serum carcinoembryonic antigen (CEA) and diioxyribonucleic acid (DNA) content of exfoliated bronchial epithelial cells
- To contrast that effectiveness with that of concomitant screening using chest x-ray and exfoliative bronchial cytology
- To determine the histological types of bronchogenic carcinoma found in steel workers and to relate these findings to the above objectives
- To examine the relationship in the development of bronchogenic carcinoma among metaplasia, dysplasia and anaplasia in exfoliated bronchial epithelial cells and to correlate the cytomorphologic findings with the DNA content (ploidy) of the cells

METHODOLOGY:

Basic biologic screening tests were performed and individual smoking, occupational and medical histories were obtained from all subjects at the implant medical facilities. Specimens and data were sent to the City of Hope Mdical Center for analysis and evaluation. The screening was performed annually or semiannually as specified by federal regulations. The screening test battery consisted of a chest x-ray and samples of sputum and blood. Statistical specificity procedures were used to evaluate the validity of these tests, and stepwise discriminant analysis was employed to evaluate their cancer screening capability over specific time periods.

PROGRESS & ACCOMPLISHMENTS:

Methods have been established for sample collection for analysis at the City of Hope Medical Center for recording and establishment of computer data files. Each coke oven was visited by project staff in order to train steel plant personnel and establish standardized methods of data collection.

The review of a sample of chest x-rays obtained from each plant was conducted to insure the technical adequacy of the films taken periodically on each worker.

In addition, various techniques for assessing the degree of polyploidy were evaluated using cytological materials from patients with lung cancer. All deaths and/or cancer diagnosis in coke workers were reported to the City of Hope Medical Center containing detailed clinical information and histologic materials.

SIGNIFICANCE TO NIOSH:

This research will be used to formulate a medical surveillance intervention and control strategy appropriate for coke oven workers, as well as for other occupational groups and those who are at high risk of developing lung cancer.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Madison, R.S., Felman, R., Mittman, C. and Afifi, A.:1979: Pulmonary Dysfunction in Coke Workers, Archives of Industrial Hygiene and Toxicology (Yugoslavia), v. 30.
- Madison, R.S., Felman, R. and Mittman, C.: 1980: Inherited Risk Factors for Chronic Lung disease, CHEST. v. 775, 2555-2575.

PERIOD COVERED: May 1, 1979 - April 30, 1980

TITLE: Epidemiological Study of Malignant Melanoma

PROJECT: 5 R01 OH00915-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Bernard Pasternack, Ph.D.
Institute of Environmental
Medicine
550 First Avenue,
New York, NY 10016

GRANTEE INSTITUTION:

New York University
Medical Center

OBJECTIVES:

- To determine the degree of association between the occurrence of malignant melanoma and possible risk factors

METHODOLOGY:

Data have been collected from New York University Medical Center. A composite risk factor score is being used to identify high risk factors of malignant melanoma. Other factors that are being studied include use of oral contraceptives, age at menarche, age at menopause, numbers of moles, tendency to freckling, and use of phenothiazines.

The data base comes from the Department of Dermatology of the New York University Medical Center. Between 1972 and 1976, data on 366 cases of primary malignant melanoma were collected by the NYU Malignant Melanoma Clinical Cooperative Group. Based on accession rates for 1974-75, it has been estimated that a total of 646 cases are available for study. The design consists of a case-control with twice as many controls as cases. The controls are patients from the same study population without malignant melanoma or other neoplastic conditions having been diagnosed.

PROGRESS & ACCOMPLISHMENTS:

Study participants have been interviewed. Participant characteristics have been analyzed according to various demographic and clinical categories and computerized. Supplemental questions were added to the original interviews in order to obtain more epidemiological data. Controls were randomly chosen from among patients 20 years of age and older appearing for a first visits. This was designed to eliminate bias due to the inclusion of long-term patients with chronic skin disease. Efforts are being made to ensure that cases and controls are being interviewed in as similar a manner as possible.

SIGNIFICANCE TO NIOSH:

The study will present a quantitative analysis of the possible effects of many factors in the etiology of malignant melanoma.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: April 1, 1979 - March 31, 1980

TITLE: Multiple Myeloma and Brain Tumors in Physicians

PROJECT: 1 R01 OH00920-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Genevieve M. Matanoski, M.D., Ph.D.
School of Hygiene & Public Health
615 North Wolfe St.
Baltimore, MD 21205

GRANTEE INSTITUTION: Johns Hopkins University

OBJECTIVES:

- To study the etiology of brain tumors and multiple myeloma and their correlation in physicians, a relatively homogeneous population distributed across the U.S.

METHODOLOGY:

The design is a case-control study with an estimated 350 cases of each of the cancers and a stratified random sample of 200 deceased controls comparable by age, race, sex, and year of death. The physicians used in this study were selected from the total physician death population over 15 years. Equal numbers of living controls were also selected.

The risk factors identified in previous studies will be examined in telephone interviews with the next-of-kin, and the physician's associates. Special emphasis will be placed on determining the exact number of years of exposure to radiation and the estimated dose levels by year or dosimetry data. Questions concerning patient contact, personal characteristics and medical history will be included. A multivariate analysis of data will be used to determine the association of each of these concerns with radiation, infection, or other factors.

PROGRESS & ACCOMPLISHMENTS:

During the first year of the study, cases of multiple myeloma and brain tumors were identified in the physician population and appropriate controls selected. A questionnaire was designed to identify exposures to radiation, infections, and other antigenic stimuli.

SIGNIFICANCE TO NIOSH:

This study provides an opportunity to identify risk factors for two cancers in a relatively homogeneous population in distributed areas of the country.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: August 1, 1979 - July 31, 1980

TITLE: An Occupational History Module for Cancer Patients

PROJECT: 1 R01 OH00960-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Lorne Houten, Ph.D.
Department of Research Medicine
Nursing Education Building
Philadelphia, PA 19104

GRANTEE INSTITUTION: University of Pennsylvania

OBJECTIVE:

- To develop and test an occupational history questionnaire, possibly computer assisted, which will collect routine occupational information and also detect data concerning specific exposures in chosen occupations and industries of suspected high risk
- To design the system to be compatible with the centralized cancer patient data system (CCPDS) currently in operation at nineteen comprehensive cancer centers
- To test the validity and reliablity of the occupational data collected by the questionnaire

METHODOLOGY:

In this investigation, the grantee will develop and test an occupational history module that will be compatible with the basic CCPDS data and can be adopted by comprehensive cancer centers, either routinely or on a site or time specific basis. The questionnaire will elicit a lifetime occupational history which will include the following information for each job: industry and occupation; dates of employment; location of employment, specific responsibilities, general description of working environment; and inquiries into any specific exposures (e.g., asbestos, and vinyl chloride). Information on smoking history will be obtained concurrently. A key feature of the occupational history will be a branching system of inquiry. If the above questions should elicit a history of employment in one of a predetermined list of specific occupations, industries or job duties, detailed inquiries will be made into both chemical and other types of exposures specific to that occupation or job.

PROGRESS & ACCOMPLISHMENTS:

A list of occupational exposures for 26 major industries has been compiled. Work has begun on development of the questionnaire including building appropriate computer software.

SIGNIFICANCE TO NIOSH:

The development of an effective occupational history module for cancer patients would be supportive of future epidemiology projects.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 1, 1979 - August 31, 1980

TITLE: Cadmium and Hypertension

PROJECT: 5 R01 OH00897-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Bohdan R. Nechay, D.V.M.
Department of Pharmacology
& Toxicology
Galveston, TX 77550

GRANTEE INSTITUTION: University of Texas Medical Branch

OBJECTIVES:

- To determine if the enhanced vascular responsiveness to norepinephrine is associated with the development of hypertension
- To define a cadmium exposure regiment which will consistently lead to increased vascular reactivity and hypertension
- To determine if the enhanced vascular reactivity includes increased responsiveness to other vasoactive agents
- To determine if there are other factors altered by cadmium such as renal salt retention
- To determine whether a genetic predisposition to hypertension influences the response to cadmium
- To establish the mechanism for vascular effect of cadmium

METHODOLOGY:

In this investigation, rats were exposed to various regiment of cadmium for periods of one week to one year. Blood pressure and vascular reactivity were measured *in vivo*. The *in vitro* work included isolated arteries removed from cadmium exposed rats as well as preparations to which cadmium was added. Part of the study was conducted on spontaneously hypertensive rats to determine the possible genetic contribution to the vascular effects of cadmium.

PROGRESS & ACCOMPLISHMENTS:

As a result of environmental exposure and stored excretion, there was a high cadmium burden in the entire population. It has been demonstrated that cadmium causes increased arterial reactivity to adrenergic stimulation in the rat. Cadmium in concentration of .075 to .25 um enhanced the pressor responses to nerve stimulation, but higher concentrations inhibited the response. The pressor response to norepinephrine was inhibited by cadmium but required a concentrations 100 x higher than that needed for inhibition of the response to nerve stimulation. Then dual effect of cadmium on the response to nerve stimulation suggests a plausible explanation for conflicting reports in the literature regarding the blood pressure effects of cadmium exposure. Enhancement of the response to nerve stimulation by low concentrations of cadmium provides a possible mechanism for cadmium induced hypertension.

SIGNIFICANCE TO NIOSH:

The results from these studies should provide information on the relationship between cadmium and hypertensive disease.

PUBLICATIONS RESULTING FROM THIS GRANT

- Williams, B.J., Laubach, D.J., Nechay, B.R., and Steinsland, O.S.:1978: The Effects of Cadmium on Adrenergic Neurotransmission in vitro. Life Sci. 23:1929-1934.
- Nechay, B.R., Williams, B.J., Steinsland, O.S., and Hall, C.E.:1978: Increased Vascular Response to Adrenergic Stimulation in Rats Exposed to Cadmium. J. Toxicol. Environ. Health 4:559-567.
- "Bimodal Effect of Cadmium on Aortic Calcium or Magnesium Adenosine Triphosphatase Activity" Fed. Proc. 1980

PERIOD COVERED: April 1, 1979 - March 31, 1980

TITLE: Job Conditions, Occupation, and Coronary Heart Disease

PROJECT: 1 R01 OH00906-01

PRINIPAL INVESTIGATOR & ADDRESS: Robert A. Karasek, Ph.D.
Room 302
Seeley Mudd Bldg.
New York, NY 10027

GRANTEE INSTITUTION: Columbia University

OBJECTIVE:

- To examine U.S. data on cardiovascular disease (CVD) and job conditions for associations similar to those recently obtained in cross-sectional and prospective analysis of Swedish national data

METHODOLOGY:

This investigation examined five major U.S. data bases, the Health Interview Survey (1972); Health Examination Survey (1960-62); Health and Nutrition Examination Survey (1970-75), The Western Collaborative Study, and The Exercise Heart Study (1971-1975). While data measuring job characteristics are generally weak in existing large scale U.S. CVD - Coronary heart disease data bases, the above surveys contain either limited direct measures of the relevant job characteristics or detailed U.S. Census Occupational Codes (441) categories. These codes were used to indirectly assess job condition impacts with the help of job characteristics occupational data in three national U.S. working conditions surveys (1969, 1972, and 1977).

PROGRESS & ACCOMPLISHMENTS:

The analysis of data on a representative sample of the Swedish male work force showed a consistently strong association between validated reports of CVD and job conditions in two Swedish cross-sectional studies and in a prospective study. These findings supported earlier studies which all observe an association between either job work load, job skill level or job decision latitude measures and CVD.

The model, based on work environment conditions, represents an alternative psycho-social mechanism of disease development similar to that implied by current "Type A" personality characteristics research. Symptoms are most prevalent among workers with low decision latitude on the job and high psychological job demands. Illness risk with high job demands is stronger at low levels of job discretion than in high levels.

SIGNIFICANCE TO NIOSH:

Current U.S. data bases do not provide reliable or complete information to support a final assessment of job related CVD risk. This project, through maximum use of extensive existing data resources, should provide a basis for development of more exact data collection instruments in the future. Project findings should include a recommended job analysis instrument, as well as a discussion of detailed occupational categories presently at risk in this country.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: July 1, 1979 - June 30, 1980

TITLE: Back Injuries: Mechanical Stress in the Human Spine

PROJECT: 2 R01 OH00514-06

PRINCIPAL INVESTIGATOR & ADDRESS:

Albert B. Schultz, Ph.D.
Chicago Circle
Box 4348
Chicago, IL 60680

GRANTEE INSTITUTION: University of Illinois

OBJECTIVES:

- To develop a fundamental understanding of the mechanics of various lifting and manual materials handling tasks
- To extend existing models of the skeletal spine and of intervertebral discs to achieve a capability to analyze manual materials handling task mechanics
- To validate the models to the extent feasible
- To use the models to determine the magnitudes of the forces, moments, and stresses acting within the spine during the execution of representative tasks
- To relate these findings to the industrial back injury problem and programs for its solution

METHODOLOGY:

This investigation utilized both live human subjects and human cadavers. Pure single mode loadings were applied to the compressively preloaded, but otherwise unconstrained superior vertebra. Six displacements/rotation response components were measured using six dial gauges, and intradiscal pressure measured with a transducer-tipped hypodermic needle. Disc and end-plate bulge measurements were made with small strain-gauge displacement transducer. Posterior and posterolateral disc bulges were also measured. Response under large compressive loads will be tested using an instron or an MTS testing machine for load application. The significance of anatomical variables to workers injury risk will be noted. These would include both gross variables, such as sex and body build, and also smaller details, such as intervertebral disc heights.

PROGRESS & ACCOMPLISHMENTS:

Body dynamics were studied during repetitive lifts in sagitally-symmetric configurations. Kinematic data were acquired using optoelectronic cameras. These data are now being processed.

Mathematical models, employing rigid-body equilibrium concepts, were developed to predict spine loads. Myoelectric measurements were made in a number of representative work situation in several groups, each consisting of ten healthy young male adults.

Voluntary trunk strengths in pure twisting and in direct shoulder compression lifts were made in 58 healthy males and 79 healthy females whose ages ranged from 15 to 65 years.

Further development and testing of a finite-element model suitable for anaylysis of stresses imposed by compressive loading continued. The effects of disc gross geometry, nuclear integrity, and annular material properties of mechanical behavior were predicted and reported.

SIGNFICANCE TO NIOSH:

The results of these studies could provide information which might be used to reduce the incidence and severity of industrial back injuries. This information would identify task situations that are high risk and contribute to guidelines for objective evaluations of compensation claims.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Shultz, A.B., Warwick, D.N., Berkson, M.H., and Nachemson, A.L.:1979: Mechanical Properties of Human Lumbar Spine Motion Segments. Part I: Responses in Flexion, Extension, Laterial Bending, and Torsion, Journal of Biomechanical Engineering, 101:46-52.
- Berkson, M.H., Nachemson, A.L., and Schultz, A.B.:1979: Mechanical Properties of Human Lumbar Spine Motion Segments. Part II: Responses in Compression and Shear; Influence of Gross Morphology, Journal of Biomechanical Engineering 101:53-57.
- Nachemson, A.L., Schultz, A.B., and Berkson, M.H.:1979: Mechanical Properties of Human Lumbar Spine Motion Segments. Part III: Influences of Age, Sex, Disc Level, and Degeneration, Spine 4:1-8.
- Andersson, G.B.J., Schultz, A.B.:1979: Effects of Fluid Injection in Mechanical Properties of Intervertebral Discs, Journal of Biomechanics 12:453-458.
- Andersson, G.B.J., and Schultz, A.B.:1979: Transmission of Moments Across the Elbow Joint and the Lumbar Spine, Journal of Biomechanics 12:747-755.
- Takashima, S.T., Singh, S.P., Haderspeck, K.A., and Schultz, A.B.:1979: Model for Semi-Quantitative Studies of Muscle Actions, Journal of Biomechanics 12:929-939.
- Schultz, A.B., Liu, W., and Novak, G.:1979: A Scheme of Analysis of the Mechanics of the Lower Trunk During Manual Materials Handling, 1976 International Symposium (NIOSH): Safety in Manual Materials Handling, 78-81.

- Andriacchi, T.P., Hampton, S.J., Schultz, A.B., and Galante, J.O.:1979: Three-Dimensional Coordinate Data Processing in Human Motion Analysis, Journal Of Biomechanical Engineering 101:279-283.

- Warwick, D., Novak, G., Schultz, A.B., and Berkson, M.:1980: Maximum voluntary Strengths of Male Adults in Some Lifting, Pushing and Pulling Activities, Ergonomics 23:49-54.

- Andersson, G.B.J., Ortengren, R., and Schultz, A.:1980: Analysis and Measurement of the Loads on the lumbar Spine During Work at a Table, Journal of Biomechanics 13:513-520.

- Spilker, R.L.: Mechanical Behavior of a Simple Model of an Intervertebral Disk Under Compressive Loading, Journal of Biomechanics. In press.

- Spilker, R.L.:Improved Hybrid-Stress Axisymmetric Elements Including Behavior for Nearly Incompressible Materials, Int. J. Num. Methods in Engng. In press.

PERIOD COVERED: February 1, 1980 - January 31, 1981

TITLE: An Investigation of Occupational Wrist Injuries in Women

PROJECT: 3 R01 OH00679-04

PRINCIPAL INVESTIGATOR & ADDRESS:

Thomas Armstrong, Ph.D.
2260 G. Brown Laboratory
Ann Arbor, MI 48109

GRANTEE INSTITUTION: University of Michigan

OBJECTIVE:

- To determine if findings from previous studies can be used to modify work methods, in order to alleviate the carpal tunnel syndrome (CTS)

METHODOLOGY:

Three different approaches were used in this investigation. They include:

- A diagnostic test battery evaluation of 30 patients with advanced CTS to determine the sensitivity, specificity, and predictive value of each test in the battery
- An intervention study which included the following:
  - The effect of worker pacing versus job paced work on the prevalence of CTS,
  - The effect of wearing wrist splints on CTS
  - Evaluation of the effects of summer layoff for model change in hand performance on CTS,
- Anatomical study preparation of 2 additional hands for a histological analysis and analysis of the relationship between hand geometry and histology

PROGRESS & ACCOMPLISHMENTS:

A series of "pace" and "splint" studies was conducted to demonstrate the use of the test battery for monitoring the condition of workers' hands, as various employer interventions were introduced into the work activities. The data from these studies were analyzed by standard stastistical methods. A significant difference was found between the median and ulnar motor latencies. Some important trends cited were:

- Average test scores for successive weeks before the first shifts demonstrated no difference. This indicates that the subjects' hands tended to recover over the weekends to the same starting condition before the paced and non-paced trials

- The average of all test scores after the first shift are better following work at paced and non-paced trials

- The exception is the median versus ulnar two point discrimination score; this average score following paced work is slightly greater than unpaced work

- The average subject performance was better at the beginning of the splint trial following the week of work without the spint

- Average median and ulnar motor latency scores were significantly better before work with the splint

SIGNIFICANCE TO NIOSH:

The results of intervention studies promote uniform pacing of work as a CTS central measure; the treatment of CTS and cumulative trauma disorders in industry as a management tool; and the evaluation and demonstration of conditions over time in varied work settings with minimum management of industrial CTS workers.

The anatomical study provides a physiological and biomechanical basis for understanding the relationship between executions with certain hand postures and cumulative trauma to underlying tissues.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Armstrong, T., Chaffin, D. and Foulke, J.: 1979: "Methodology for Documenting Hand Positions and Forces During Manual Work." J. Biomech., 12:131-133.

- Armstrong, T., Chaffin, D. and Foulke J.: 1979: "A Method for Measuring Shapes of Anatomical Surfaces." J. Biomech., 12:397-399.

- Armstrong, T. and Chaffin, D.: 1979: "Some Biomechanical Aspects of the Carpal Tunnel." J. Biomech. 122:567-570.

- Armstrong, T. and Chaffin, D.: 1979: "Carpal Tunnel Syndrome and Selected Personal Attributes." J. Occ. Med., 21:481-486.

- Goldstein, S.A., Armstrong, T.J., Chaffin, D.B., and Maithews, L.S.: Biomechanics or Repetitive Trauma to the Upper Extremities, Presented at the Orthopedic Research Society. In press.

PERIOD COVERED: May 1, 1979 - November 30, 1980

TITLE: Vibration and Industrially Related Low Back Disease

PROJECT: 2 R01-OH00745-03

PRINCIPAL INVESTIGATOR & ADDRESS:

John Frymoyer, M.D.
Department of Orthopaedic
Surgery
Burlington, VT 05401

GRANTEE INSTITUTION: University of Vermont

OBJECTIVES:

- To clarify mechanical factors responsible for low back pain through retrospective and prospective studies
- To perform a survey of a general practice population to determine the incidence of low back disorders

METHODOLOGY:

Six study populations will be selected with various mechanical risk factors, and will be studied through questionnaires, psychological evaluation, and physical examination. The questionnaire will determine (1) episodes of low back pain not requiring treatment, (2) episodes treated by other health care professionals (3) disability resulting from the pain, and (4) any occupational stresses such as vibration or heavy lifting.

For the retrospective study, the investigators will attempt to define age-matched volunteers from the six male population subgroups that can be used for the prospective study: those with a history of low back pain, both with and without identifiable mechanical risk factors, who have required medical attention; and those without identifiable mechanical risk factors who have never had any low back pain.

This study involves five steps giving all volunteers: (1) a computerized questionnaire, (2) a standard physical examination, (3) taking AP and lateral spine radiographs (4) doing biochemical studies, and (5) studying individual case histories.

PROGRESS & ACCOMPLISHMENTS:

Over 200 patients have been tested biomechanically, psychologically, and by questionnaires. A mini Minnesota Multiphasic Personality Inventory (MMPI) has been developed and validated. The diagnostic subgroups demonstrate significant differences in biomechanical tests. The biomechanical and psychological tests show significant relationships. A spine stiffness apparatus has been developed and the use of stereoradiographs for segmental instability have been developed. In addition, highly significant relationship were identified between low back pain and psychological stress, vibration, other risk factors and smoking. A laboratory vibrational tester was completed which is capable of 0-20 Hertz and 6 inch displacements. A study of the sacroiliac joint and its function in vibration absorption has been completed.

SIGNIFICANCE TO NIOSH:

It is expected that mechanical factors responsible for low pack pain will be clarified. A better definition of risk factors may be identified and safety recommendations may be given for vibrational loading.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Frymoyer, J.W., Pope, M.H., Wilder, D.G., Stiokes, I.A., Moreland, M. 1979. Moire Fringe Topography of the Human Body. Presented and published as Abstract at 31st ACEMB. Pending publication in Medical Instrumentation.
- Pope, M.N. Buturla, E., Wilder, D.G., Frymoyer, J.W. 1979. Changes in the Form of the Lumber Spine. Accepted by 7th Annual N.E. Bioengineering Conf.

PERIOD COVERED: June 1, 1980 - May 31, 1981

TITLE: Methods for Reducing Exposure to Cotton Dust

PROJECT: 5 R01 OH00744-02

PRINCIPAL INVESTIGATOR & ADDRESS: Solomon P. Hersh, Ph.D.
PO Box 5006
Raleigh, NC 27650

GRANTEE INSTITUTION: North Carolina State Universtiy

OBJECTIVES:

- To investigate effective and less costly methods for reducing cotton dust concentration in the cotton textile industry
- To evaluate the effectiveness of various dust sampling devices
- To provide well documented dust samples for etiological studies by other investigators

METHODOLOGY:

Cotton was processed in an isolated model card room. Measurements were taken of the dust concentration generated in the room. A large variety of aerosol samplers, and collections were made of the airborne respirable cotton dust for study by other investigators. Cottons of known genetic, growing, cultivating, harvesting, ginning, and processing history were processed to determine the influence of these factors on dust concentrations. Intervention studies are also being carried out, and the influence of blending with synthetic fibers will be examined.

PROGRESS & ACCOMPLISHMENTS:

The ongoing study of the effect of washing cotton (post-ginning) was completed. It was concluded that washing decreases the dust emitted at the carding stage. The effect of harvesting cotton with different types of mechanical pickers on the dust produced during processing was investigated. Preliminary results that the spindle picker generates less dust during carding than the brush stripper harvester.

Bales of cotton were processed to provide dust samples for gram negative bacterial count. Experiments to evaluate the effect of additives on the dust emission in carding are underway.

SIGNIFICANCE TO NIOSH:

This research may result in more cost effective methods for complying with standards for occupational exposure to cotton dust.

Approaches will be evaluated for more effectively controlling exposure to cotton dust in order to further reduce the health hazards.

PUBLICATIONS RESULTING FROM THIS GRANT:

- R.H. Johnson, Jr., S.P. Hersh, S.K. Batra, and T. Myers. Evaluation of Cleaning and Washing Processes for Cotton Fiber: Part III: Carding and Dust Levels," in Textile Research Journal, In press.

PERIOD COVERED: January 1, 1979 - December 31, 1980

TITLE: Sampling Efficiencies of Personal Particulate Samplers

PROJECT: 5 R01 OH00774-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Klaus Willeke, Ph.D.
3223 Eden Avenue
Cincinatti, OH 45267

GRANTEE INSTITUTION: University of Cincinnati

OBJECTIVE:

- To determine the overall sampling efficiencies of inlets as a function of particle size, particle adhesion, ambient air velocity and inlet orientation relative to the ambient air flow direction

METHODOLOGY:

The testing was performed in a low speed wind tunnel with a 40 cm x 50 cm test section. The wind tunnel was modified for these tests. The aerosols will be generated by a vibrating orifice monodisperse aerosol generator and will be charge-neutralized by a krypton-85 audioactive source. The generator is capable of generating particles from about 1 to over 50 um in diameter, and will be modified for use in the wind tunnel. The aerosols were mixed with the airstream only over the region of testing. Uniformity of concentration will be tested by translating a 130 kinetic sampler across the test region. The test inlets will be adjustable to desired angles relative to the flow axis.

PROGRESS & ACCOMPLISHMENTS:

The construction of the wind tunnel and associated equipment was completed.

SIGNIFICANCE TO NIOSH:

This project will evaluate the particle sampling efficiency of personal sampler inlets and determine the ranges for which sampling is imperfect relative to sampling flow rate, sampler orientation, ambient wind velocity, particle size and particle adhesive properties. In addition to identifying the limitations of existing inlet configurations, the experience gained may be used in the improvement of inlet geometrics.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 1, 1979 - August 31, 1980

TITLE: Control of Volatile Materials in Surface Coatings

PROJECT: 5 R01 OH00838-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Charles E. Feigley, Ph.D.
School of Public Health
Columbia, SC 29208

GRANTEE INSTITUTION:

University of South
Carolina

OBJECTIVES:

- To develop methods for estimating ventilation requirements for the controlling the toxicity and explosion hazards resulting from volatile release from surface coatings
- To develop an apparatus capable of measuring volatile evaluation rates from coded surfaces
- To study the evolution of volatile materials from a common coding material under varying conditions of temperature, humidity air flow across the surface, and coding thickness
- To develop techniques by which these findings can be applied in realistic work situations to specify control requirements

METHODOLOGY:

Investigators are studying rates of evolution of volatile materials from surface coatings during the drying period following coating application, and the application of experimental findings to the development of means to control exposures in work situations. Vapor analyses will be conducted by infrared absorption spectrometry and gas chromatography with flame ionization.

A humidity and temperature controlled air stream is passed over a coded surface. Individual volatile species are measured using infrared spectroscopy and gas chromatography.

PROGRESS & ACCOMPLISHMENTS:

In the first year, investigators performed a literature search, constructed the experimental apparatus and characterized mass transfer within the experimental apparatus.

An apparatus for the measurement of volatile loss from coated surfaces was developed. A series of preliminary experiments were performed using chips of plywood coated by brush with shellas. It was observed that these rates reached the theoretical maximum evolution rate for a brief period. Rates then declined until the entire surface was dry. This corresponded to a 90 percent loss of ethanol. A dramatic effect of both air velocity and coding thickness on the rate of volatile release was observed.

SIGNIFICANCE TO NIOSH:

The application of surface coatings can result in conditions that are hazardous to health, such as explosion and chronic and acute toxicity. This project is the initial research effort to address the fundamental physical processes which influence the rate of volatile evolution for control purposes.

PUBLICATIONS RESULTING FROM THIS GRANT:

- C.E. Feigley and H.E. Jeffries.:1979: Analysis of Processes Affecting Oxidant and Previsions in the Los Angeles Reactive Pollutant Program (LARPP) Operation 33, Atmospheric Environment 13, p. 1369.

PERIOD COVERED: April 1, 1979 - March 31, 1980

TITLE: Developing Cotton Cultivars With Caducous Bracts

PROJECT: 5 R01 OH00860-02

PRINCIPAL INVESTIGATOR & ADDRESS: Hiroshi Muramoto, Ph.D.
Plant Sciences Department
Tucson, AZ 85721

GRANTEE INSTITUTION: University of Arizona

OBJECTIVES:

- To transfer the caducous bract characteristic to cotton cultivars
- To learn how the trait is inherited and how and why bracts fall before the bolls open

METHODOLOGY:

Selection in the caducous bract cotton at the hexaploid level will continue with emphasis on caducous bract and productiveness. This investigation uses three methods: 1) Back crossing program using G. hirsutum and several crosses between DPL-16, DPL-61, Acala 6608, Arizona Superokra No. 1 and Stoneville 213; 2) Crossing of hexaploids G. armourianum and G. sturtianum with G. hirsutum and 3) Cross between G. hirsutum and G. armourianum with G. herbaceum.

PROGRESS & ACCOMPLISHMENTS:

The back crossing program is progressing on schedule with several pentaploids growing in the field. Seeds from these plants will be harvested and progenies will be grown next season.

SIGNIFICANCE TO NIOSH:

Water extracts of dried bracts are known to cause byssinotic symptoms, by eliminating the bracts cleaner cotton and a reduction in the incidence of byssinosis may result.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 28, 1979 - August 31, 1980

TITLE: Control Technology Demonstration - Furniture Industry

PROJECT: 5 R01 OH00953-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Franklin D. Hart, Ph.D.
Center for Acoustical
Studies
Raleigh, NC 27650

GRANTEE INSTITUTION: North Carolina State University

OBJECTIVES:

- To provide a fully documented demonstration of feasible control technology for reduction of noise from woodworking machinery in the furniture and wood products industries
- To utilize economic and technological factors to provide information for assessing the overall effectiveness of control measures

METHODOLOGY:

This project involved the selection of a factory, assessment of the noise environment to be carried out in-plant, selection of effective technologies for noise control, implementation of control measures, assessment of achievable noise reduction and cost impact, preparation and dissemination of a report documenting the technology and procedures employed, the reduction in hazardous exposure achieved, and a detailed cost impact accounting. A one-day seminar on the program and its results will be presented to industry and government representatives.

PROGRESS & ACCOMPLISHMENTS:

A demonstration facility was selected and the noise environment at the furniture company was assessed. Contour maps were constructed for various operating circumstances. A machine ranking has been developed after assessing noise severity, number of employees exposed, and location of the worst noise sources. Selection of noise control technology has been completed for several machines and is continuing. Implementation of noise control technology has been initiated on each machine for which technology selection has been completed.

Progress made to date on this project tends to substantiate the hypothesis that engineering control is a viable option for protecting the hearing of workers in the furniture industry.

SIGNIFICANCE TO NIOSH:

This project will assist NIOSH in assessing the control technology portion of noise standards, including cost and technological considerations.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 28, 1979 - August 31, 1980

Control Technology/Safety/
Engineering Controls
Development/Testing

TITLE: Design and Demonstration of a Ventilation System

PROJECT: 5 R01 OH00959-02

PRINCIPAL INVESTIGATOR & ADDRESS:
Robert J. Heinsohn, Ph.D.
301 Mechanical Engineering
Building
University Park, PA 16802

GRANTEE INSTITUTION: Pennsylvania State University

OBJECTIVES:

- To design and demonstrate an industrial ventilation system for portable grinding and welding
- To develop computer-aided design programs for use by engineers in designing similar ventilation systems

METHODOLOGY:

This investigation involves the design and construction of a ventilation system and demonstration of its effectiveness through experimentation; development of computer codes with provisions for shape, work piece, and work tools; development of computer codes that can predict air velocity, air supply rate and "push pull" flow rate; development of a computer code to predict contaminant concentrations at various given locations and to predict trajectories of grinding particles and rate of particle generation; and, combination of the above computer codes into a single program which will enable engineers to design other systems.

PROGRESS & ACCOMPLISHMENTS:

A ventilation system design has been partially tested in the laboratory and will be further tested in actual work places. Air flow through the hood was modeled as two dimensional, invisible and incompressible. A computer code was written that predicts the velocities at preselected nodes within the booth.

SIGNIFICANCE TO NIOSH:

This approach is likely to provide speed in the design and assessment of various ventilation systems, as well as in predicting their performance. Increased accuracy and precision for the computations is expected. This would allow for easy demonstration in industry of available technology and feasible engineering controls which promote more healthful work environments.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 30, 1979 - August 31, 1980

TITLE: Removal of Contaminating Liquids from Surfaces

PROJECT: 1 R01 OH01004-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Stanley Middleman, D. Eng.
Room 5262 Urey Hall
La Jolla, CA 92093

GRANTEE INSTITUTION: University of California

OBJECTIVE:

- To develop an experimental and theoretical understanding of the mechanics of removal of a contaminating liquid from a solid surface

METHODOLOGY:

Thin liquid films will be deposited on a variety of solid surfaces and then removed by the shearing and impaction of liquid jets. Techniques for measuring the rate of removal of a film from a surface will be developed. Mathematical models will define an efficiency that characterizes the flushing system, the contaminating layer, and the contaminated surface. Secondary recontamination by splashing and/or contaminant aerosol formation will be studied. Theoretical models will aid in the interpretation and correlation of observations.

PROGRESS & ACCOMPLISHMENTS:

This is a new grant. Progress and accomplishments will be reported in the FY81 grant report.

SIGNIFICANCE TO NIOSH:

This research is expected to result in greater knowledge in the area of decontamination after spills and leaks. In addition, the results may have even greater applicability to routine operations such as cleaning process vessels, maintenance cleaning, and parts cleaning in the manufacturing process.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date.

PERIOD COVERED: August 1, 1980 - July 31, 1981

blank page

NIOSH DERMATOLOGY GRANT PROGRAM

On January 3, 1980 NIOSH initiated the active solicitation of research and demonstration grants in the area of occupational cutaneous hazards and diseases. NIOSH expects to award up to $2 million over a three-year period of this on-going program. The standard National Institutes of Health (NIH) application and review procedures are followed in all NIOSH grants programs.

BACKGROUND

The most pervasive current occupational health problem in the United States is widespread, debilitating, work-related skin disorders. More people suffer from occupational skin disorders than any other single category of occupational disease in America. The Bureau of Labor Statistics (BLS) has reported that skin diseases and disorders have accounted for more than 40 percent of all reported occupational diseases in recent years. Moreover, inadequate reporting masks the true incidence, which is suspected to be from 10 to 15 times greater than reported in the BLS data. Today, it is generally accepted that these disorders impose a serious personal and economic burden in terms of lost production, lost wages, increased medical costs, family disruption, personal discomfort, and ill health.

Intensive scientific investigation is needed in a number of scientific and technological areas relative to workplace skin hazards.

RESEARCH GOALS AND SCOPE

The goal of this program is to encourage high quality research and demonstration grants in specific domains.

DATA SYSTEMS RESEARCH

Projects to identify the potential extent and societal impact of occupational skin diesease -

- Develop a unified data collecting system that will properly identify high risk industries, processes, and agents. The system should possess: (1) a process-specific classification; (2) a specific hazardous substance file; (3) a specific hazardous physical process file; and (4) a system for correlating 1,2, and 3.

BIOCHEMICAL AND PHYSIOLOGICAL RESEARCH

Studies to elucidate the nature of occupational skin disease -

- Develop new models for studying percutaneous absorption and estimating systemic uptake. These models should focus and elucidate the biochemical and physiological aspects of penetration as they may be affected by hydration, organic solvents, age, and by the physiochemical characteristics of the penetrant

- Elucidate the structural (cellular) and biochemical aspects of non-allergic inflammatory reactions (direct irritation)
- Determine differences in pathophysiologic patterns as influenced by molecular characteristics of the irritant, rates of penetration, metabolism, lysosomal and kinin activities. These characteristics should be correlated with irritant capacity and type of irritant damage
- Examine the action of marginal irritants on cell organelles
- Determine the cellular and biochemical, or metabolic factors associated with the "turning off" of the inflammatory response on continued exposure
- Determine the long-term cutaneious effect of polychlorinated biphenyls and dioxins in humans
- Determine the biologic mechanisms involved in the pathogenesis of adverse skin effects of acnegenic agents, such as PCBs, dioxins, and dibenzofurans. Attention should be given to the action of such agents and metabolities on sebaceous cells, on keratinocytes, on lipid metabolism, on cutaneous flora which produce lipolytic enzymes, on endocrine activity (including direct or indirect adrogenic effects), and on pigmentation and its relation to prophyrin metabolism and ultraviolet radiation reactivity

EPIDEMIOLOGICAL RESEARCH

Studies which consider the epidemiology of occupational cutaneous diseases -

- Determine the long-term cutaneous effect of polychlorinated biphenyls and dioxins in humans
- Determine the chronic effects, particularly those relating to skin, of exposure of workers and their families to 2, 3, 7, 8, tetrachlorodibenzodioxin in the last thirty years
- Examine the dermatolcgical manifestation of other occupational illnesses
- Determine systemic manifestation (acute and chronic) of toxic substances absorbed through the skin

TEST METHODOLOGY RESEARCH

Projects to improve test methodologies and facilitate early identification of cutaneous hazards -

- Appraise current methods for predicting cutaneous hazards and develop new methods for assessing adverse effects, other than contact dermatitis or photosensitization, such as detection of marginal irritants, acnegenic substances, granulomatous agents, and pigment altering substances
- Develop research methodologies, including non-biological screening techniques, to determine the potential cutaneous hazards of all existing and new commercial substances, processes and agents

CONTROL TECHNOLOGY RESEARCH

Studies to develop new and improved methods to prevent occupational skin diseasee -

- Develop new or improved methods to prevent skin penetration by specific types of compounds
- Adapt existing methods, as well as develop new methods, of monitoring and controlling cutaneous hazards in the workplace
- Seek to use innovative approaches, such as alternative materials, engineering controls, process modification, and protective equipment to prevent occupational skin disease problems already identified, and to solve emerging problems

Dermatology/In Vivo/
In Vitro/Animal/Toxicology

TITLE: Pathomechanisms of Chemically Induced Depigmentation

PROJECT: 5 R01 OH00714-03

PRINCIPAL INVESTIGATOR & ADDRESS:

Gerald A. Gellin, M.D.
Department of Dermatology
San Francisco, CA 94143

GRANTEE INSTITUTION:

University of California-
San Francisco

OBJECTIVES:

- To investigate depigmenting actions of chemicals on mammalian skin observed in the home, community or occupational environment
- To provide information from in vivo studies on pathomechanisms of chemically induced depigmentation
- To use in vitro studies to provide: quick screening techniques for chemicals which have the depigmenting potential; and clarification of molecular biological changes which occur in both melanocytes and keratinocytes by direct contact of the chemicals

METHODOLOGY:

This study used black guinea pigs and black mice as laboratory animal models. The depigmenting capacity of a variety of phonolics and catecholics, and their congers was studied using these animals. The histological, histochemical, and autoradiographic examination of normal, irritated and depigmented animal skin with light and electron microscopy was performed.

PROGRESS & ACCOMPLISHMENTS:

Results from this study show that 4-tertiary butyl catechol (TBC) depigmentation does not occur in the pigmented ear skin of Uscd strain hairless mice. This conclusion contrasts with findings of the pigmented ear skin of guinea pigs and indicates that genetic factors are involved in TBC depigmentation. TBC reduced ultraviolet (UV) stimulated tanning, but did not decrease croton oil induced pigmentation. DOPA stained split epidermal shuts showed enlarged melanocytes with thick dendrites.

After UV followed croton oil, some of the melanocytes developed beaded dendrites and others became rounded. After treatments, the number of melanocytes decreased on the UV irradiated side. In contrast, after TBC application, a moderate increase of melanocytes was seen in the croton oil treated mice. The results suggest that differential effects of TBC occur on melanocytes and seem to depend upon their morphology and functional states.

TBC does not reduce the number of melanocytes and does not cause depigmentation in the ears, whereas TBC not only reduces the UV pigmentation, but also prevents tanning.

Findings indicate that TBC promotes a step of melanoogenesis and that TBC pigmentation does not appear to be due to enzyme competition.

SIGNIFICANCE TO NIOSH:

Through the application of basis scientific techniques to the problem of occupationally induced depigmentation, this study may open a new avenue for molecular biologists and other experimental biologists to become involved in the investigations of other occupational diseases.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Hoshino, S., Gellin, G.A., Epstein, J.H. and Fukuyama, K.: 1979: Effects of 4-tertiary butyl catechol (TBC) on melanocytes (MC) in hairless mice. Clin. Res. 23:18A.
- Hoshino, S., Gellin, G.A. and Epstein, J.H.: 1979: 4-tertiary butyl catechol (TBC) effects on UV and croton oil (CO) induced melanocytes (MC). J. Invest. Dermatol. 72/4:207-208.
- Creasey, A.A., Hackett, A., Smith, H., Fukuyama, K. and Epstein, W.: 1979: In vitro and in vivo characterization of human melanoma cells. In Vitro. In Press.
- Gellin, G.A., Maibach, H.I., Miasiaszek, M.H. and Ring, M.: 1979: Detection of environmental depigmenting substances. J. of Contact Dermatitis. In Press.
- Gellin, G.A.: 1980: Occupational Leukoderma: In vivo and in vitro studies. Fourth Conference on Cutaneous Toxicity, Washington, D.C.

PERIOD COVERED: July 1, 1979 - June 30, 1980

TITLE: Occupationally-Induced Isocyanate Reactions

PROJECT: 5 R01 OH00773-02

PRINICIPAL INVESTIGATOR & ADDRESS:

Leonard I. Bernstein, M.D.
231 Bethesda Avenue
Cincinatti, OH 45267

GRANTEE INSTITUTION:

University of Cincinatti
Medical Center

OBJECTIVES:

- To develop appropriate animal models of isocyanate-induced hypersensitivity responses

METHODOLOGY:

This study will develop better methods of preparing and characterizing various monomeric and polymeric compounds which are formed during the reaction of isocyanates with protein carriers. The ability of monominc isocyanate protein conjugates to induce homo cytotrophic antibody and IgG immune responses in mice, rabbits and guinea pigs was studied by standard immunologic methods. Induction of cell mediated immunity by these substances will be studied by delayed type skin testing and the macrophage inhibitory factor test in guinea pigs. In addition, induction of contact dermatitis by various isocyanate compounds applied directly to guinea pig skins will be attempted.

PROGRESS & ACCOMPLISHMENTS:

This investigation has established that proper chemical characterization and stability of immunizing magnets is essential. The development of better methods for preparing and characterizing various monomeric and polymeric compounds which are formed during the reaction of isocyanates with protein carriers has begun. Physiological effects of sublethal elicting doses of various antigens are being monitored by compliance and resistance measurements in actively and passively immunized guinea pigs.

SIGNFICANCE TO NIOSH:

This study may provide information on the significance of immunologic reactions induced by isocyanate compounds. This investigation may also conclusively demonstrate whether toluene diisocyanate and hexamethylene diisocyanate induce immunoreactivity in both humans and animals.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Tse, CST; Chen, S.E., Bernstein I.L.:1979: Induction of Murine Reagenic Antibodies by Toluene Diisocyanate: An Animal Model of Immediate Hypersensitivity Reactions to Isocyanates: Am. Rev. Resp. Dis. 120:829-835.
- Tse, CST; Pesce, A.J.:1979: "Chemical Characterization of Isocyanate-Protein Conjugates," Toxicology and Applied Pharmacology, 51:39-46.

PERIOD COVERED: July 1, 1979 - June 30, 1980

TITLE: The Role of Atopy in Occupational Skin Disease

PROJECT: 1 R01 OH00954-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Edward Shmunes, M.D.
School of Health
Columbia, SC 29208

GRANTEE INSTITUTION:

University of South
Carolina

OBJECTIVES:

- To examine the role of atopy in occupational dermatitis
- To examine the delivery of effective dermatologic intervention at the time of the active case of occupational dermatitis

METHODOLOGY:

This study is investigating the incidence of atopy among 500 individuals who have closed cases of workmen's compensation in South Carolina for the fiscal year July 1, 1978 to June 30, 1979. Two questionnaires were designed for selected cases. One questionnaire was designed to determine the following:

- The degree of awareness of the atopic state in hiring and placement and whether or not such information is asked on applications
- The availability of in-plant trained personnel at the site of the closed cases of occupational skin disease
- The referral from the plant to medical care in terms of availability, degree of specialty training and internal before referral
- To determine other contributing factors such as nature of in-plant irritant or allergen, pre-existing dermatitis, and use of personal protective products on clothing

A second questionnaire was sent to the employees who represented closed cases during the specific time period and will determine family history and case history of the employees.

PROGRESS & ACCOMPLISHMENTS:

An employer questionnaire was sent to a sample of the plants in which one or more closed cases of occupational skin disease occurred. An employee questionnaire was sent to a sample of 500 of the closed cases of work related skin disease. In addition, an abstraction form was developed for the record review of all closed cases (961) of work related skin disease during the fiscal year July 1, 1978 - June 30, 1979.

Computer input of the data from the abstracts of the records of the entire caseload of work-related skin disease was gathered. An analysis of the data obtained from the abstracts of the 961 cases of work-related skin disease was completed.

Finally, 50 employer and employee questionnaires were mailed as a pilot test to determine potential problems before the mailing out of the remaining 450 questionnaires.

SIGNIFICANCE TO NIOSH:

This study should provide data on the role of atopy in occupational dermatitis and should provide information which would contribute to the delivery of effective dermatological interventions.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Shmunes, E.:1980: The Importance of Pre-Employment Examination in the Prevention and Control of Occupational Skin Disease. Journal of Occupational Medicine, v. 22:407-409.

PERIOD COVERED: December 1, 1979 - November 30, 1980

Dermatology/Cancer/Clinical Study

TITLE: Skin Effects of Chemical Exposure in Rubber Workers

PROJECT: 1 R01 OH01023-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Barbara Hulka, M.D., M.P.H.
Occupational Health Studies Group
NCNB Plaza, Suite 32
137 E. Franklin Street
Chapel Hill, NC 27514

GRANTEE INSTITUTION: University of North Carolina

OBJECTIVES:

- To determine if squamous cells carcinoma cases have been employed in the rubber industry for a longer period of time than suitably chosen controls
- To determine any differences in past exposure to polycyclic aromatic hydrocarbons between squamous cell carcinoma cases and suitably chosen controls
- To determine any differences between squamous cell carcinoma cases and controls in exposure to work areas or processes where exposure to polycyclic aromatic hydrocarbons cannot be implemented

METHODOLOGY:

A case control study of squamous cell skin cancer in 68 male rubber workers will determine if the occurence of squamous cell skin cancer is associated with past exposure to polycyclic aromatic hydrocarbons which are present in the raw materials of rubber manufacture, and associated with other risk work areas or processes on with the rubber manufacturing industry in general. Work histories of the cases and the controls will be compared to determine if the cases had a common occupational exposure which the controls did not share. A cohort of approximately 15,000 rubber workers in two rubber manufacturing companies has been identified by the Occupational Health Studies Group (OHSG) as eligible for this study. A series of 68 skin cancer cases diagnosed between 1964-1973 have been abstracted from the tumor registries of the four major Akron, Ohio hospitals. Males between 40-84 years of age who were active or retired hourly rubber workers on 11/1/64 are being studied. The first control series consists of four controls matched to each case on company, sex, race, year of birth (plus/minus 2 years), and year hired (plus/minus 2 years). In addition, the control is required to have worked until the case's date of diagnosis or date of retirement. These criteria ensure that the cases and controls will have worked during the same time period and for the same amount of time. The second control series consists of four controls matched to each case in company, sex, race and year of birth (± 2 years).

Work histories are being obtained for study subjects (cases and controls) from the employing companies and coded without knowledge of study group status, as developed by the OHSG. Where necessary, these coded occupational classification groups will be subdivided to maximally distinquish jobs with exposure to polycyclic aromatic hydrocarbons (PAHs). An industrial hygiene survey was developed and conducted to specify jobs where skin contact occurs with any of the materials which normally carry PAHs. Each classification was assigned a rating of degree of exposure to PAHs by the industrial hygiene group with separate ratings for oils, waxes, carbon black and solvents. The ratings indicate exposed-not exposed and level of exposure/high medium-low-no-exposure).

Statistical analysis will utilize the two control series selected. Initial analyses will be conducted for each company separately before combining the data.

PROGRESS & ACCOMPLISHMENTS:

The industrial hygiene survey to evaluate job categories and locations where workers may have been exposed has been completed. The majority of work histories have been coded, key punched, and stored on magnetic tape. A preliminary review of these data has begun but has not been completed.

SIGNIFICANCE TO NIOSH:

It is anticipated that this study should have immediate benefits for the population of rubber workers and ultimately for other industrial workers who are exposed to similar materials.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: August 1, 1980 - January 31, 1981

best copy available

TITLE: Chloracne: Mechanisms of Pathogenesis

PROJECT: 1 R01 OH01108-01

PRINCIPAL INVESTIGATOR & ADDRESS:

S. Madli Puhvel, Ph.D.
405 Hilgard Avenue
Los Angeles, CA 90024

GRANTEE INSTITUTION: University of California

OBJECTIVES:

- To discover the cellular biochemical events which mark the transformation of normal pilosebaceous follicles into comedones, following exposure to polycholorinated aromatic hydrocarbons
- To develop information regarding the cellular kinetics as well as the biochemical and metabolic factors involved in the development of experimentally induced chloracne

METHODOLOGY:

This investigation will use in vivo models such as the rabbit external ear and hairless mouse skin as well as in vitro studies on human balding scalp and facial skin to investigate various enzymatic and metabolic parameters which may be affected following exposure of these tissues to polychlorinated biphenyls (PCBS) and 2, 3, 7, 8-tetrachlorodibenzo-p-dioxon (TCDD). Enzymes to be assayed include transglutaminase, gamma-glutamyl transeptidase, various decarboxyloses, and aryl hydrocarbon hydroxylase. Studies of the effect of TCDD and PCB on lipid biosynthesis, which is thought to be associated with the pathogenesis of acne, will be performed on human skin. Tissue culture analysis of the effect of TCDD on in vitro growth of sebaceous follicle ductal epithelium will be analyzed. The localization of PCHs in rat skin and human skin will be investigated using radioactively labeled hexachlorphenols.

PROGRESS & ACCOMPLISHMENTS:

Progress will be reported in 1981.

SIGNIFICANCE TO NIOSH:

The development of chlorance in humans is a very sensitive indication of exposure to toxic polyhologeneted aromatic hydrocarbons. This research is likely to produce new data about the pathogenesis of chloracne which may help understand the mechanism of actions of the inducing chemicals.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 29, 1980 - August 31, 1981

Dermatology/In Vivo/
Toxicology/Human

TITLE: Photochemical Processes and Occupational Dermatoses

PROJECT: 1 R01 OH01119-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Frederick Urbach, M.D.
3322 North Broad Street
Philadephia, PA 19140

GRANTEE INSTITUTION:

Temple University
of Medicine

OBJECTIVES:

- To identify environmental and individual factors predisposing workers to light-induced skin damage
- To study the photochemistry of certain occupationally important chemical compounds with special attention to biologic consequences
- To develop standardized bioassays designed to predict dermatologic effects of chronic exposure to light and chemicals

METHODOLOGY:

This investigation consists of photochemical studies of biologically active chemicals, and studies of DNA repair of human eryphocytes in order to identify persons susceptible to photochemical injury.

PROGRESS & ACCOMPLISHMENTS:

Work has begun on the DNA studies.

SIGNIFICANCE TO NIOSH:

This research allows sampling of populations to determine the potential risk for phototoxic acute reactions and chemically augmented photocarcinogenesis. This study will identify chemicals which may pose a risk in an industrial setting.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 29, 1980 - August 31, 1981

TITLE: Accommodation and Tolerance in Humans and Guinea Pigs

PROJECT: 1 R01 OH01124-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Robert L. Rietschel, M.D.
Department of Dermatology
215 Woodruff Memorials Bldg.
Atlanta, GA 30322

GRANTEE INSTITUTION: Emory University

OBJECTIVES:

- To establish a reliable human model for the analysis of accommodation and tolerance to contact dermatitis
- To establish a reliable animal model of the human accommodation reaction
- To analyze the role of the Langerhans cell in accommodations

METHODOLOGY:

Human volunteers, half of whom have known Rhus sensitivity, will be selected for the study. The skin will be initiated with 17 percent benzalkonium chloride or 20 percent maleic acid. The subjects will then be accommodated to these materials during a period of four weeks. Responses to other agents will also be ascertained. The number of Langerhans cells in the tissue will be documented by electron and light microscopy. The accommodated skin will be analyzed for delayed hypersensitivity.

Studies on guinea pigs will follow the human studies. Mediators of inflammation will be injected into the guinea pig skin and the responses will be measured as in humans and the Langerhans. All responses to accommodation will be checked by ATPase reactions and electron microscopy.

PROGRESS & ACCOMPLISHMENTS:

Investigators are ordering materials and equipment for the study.

SIGNIFICANCE TO NIOSH:

This study is expected to lead to methods of modification of the hosts' response to irritants and allergens, and to knowledge of the mechanism of accommodation and tolerance which is relevant to the costly occupational dermatitis problem.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 29, 1980 - August 31, 1981

Dermatology/Animal/Human/
Physical Agents

TITLE: Coal Liquids: Skin Toxicity and Mutagenicity Studies

PROJECT: 1 R01 OH01149-01

PRINCIPAL INVESTIGATOR & ADDRESS:

David B. Bickers, M.D.
Cleveland V.A. Hospital
Research Building Room
10701 East Boulevard
Cleveland, OH 44106

GRANTEE INSTITUTION:

Case Western Reserve
University

OBJECTIVES:

- To identify selected topic and mutagenic consequences of exposure to specific chemical compounds (polycyclic hydrocarbons) to which workers will be exposed in coal liquefaction/gasification processes

METHODOLOGY:

Test compounds will be applied to the skin of experimental rodents. Several enzymes will be examined including arylhydrocarbon hydroxydase and epoxide hydrolase, ethoxycoumarin ethylate, and cytochrome P450. Animals will be treated with polycyclic hydrocarbons and microsomes will be prepared from their skin. The influence of these microsomes on the binding of benzo(a)pyrene and dimethylbenzathracine to DNA will be measured. The metabolism of benzo(a) pyrene and dimethylbenzanthracene by skin microsomes obtained from control animals and animals treated with cutaneous applications of polycyclic hydrocarbons will be measured using high pressure liquid chromatography. The studies will also be carried out in cultures of human skin.

The DNA altering activity of the polycyclic hydrocarbons will be tested using covalently closed circular DNA (CC DNA) to screen for DNA reactive chemical agents. DNA damage in intact human cells (fibroblasts and keratinocytes) along with exposure to a series of compounds will be measured.

PROGRESS & ACCOMPLISHMENTS:

Work has begun on screening a series of constituents that are likely to be produced in coal liquefaction/gasification processes. Preliminary studies have tentatively identified compounds that can alter enzyme activity in the skin. Mutagenicity studies have been initiated.

SIGNIFICANCE TO NIOSH:

This research is likely to lead to the identification of hydrocarbons of greater toxicity which may lead to reduced occupational hazards during the coal conversion process.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 29, 1980 - August 31, 1981

Digestive Diseases/Toxicology/
Animals/In Vitro

TITLE: Potentiation of Haloalkane Renal Injury By Ketones

PROJECT: 1 R01 OH00986-01

PRINCIPAL INVESTIGATOR & ADDRESS:

William Hewitt, Ph.D.
Dept. of Veterinary Anatomy-Physiology
College of Veterinary Medicine
Columbia, MO 65211

GRANTEE INSTITUTION:

University of
Missouri-Columbia

OBJECTIVES:

- To extend the hypothesis of Plaa and Hewitt that ketogenic chemicals will increase the susceptibility of the kidney to the toxic actions of halogenated hydrocarbons
- To determine why ketones potentiate chloroform toxicity

METHODOLOGY:

Several types of experiments are involved in this study. In the first, the potentiating activity of ketones of varying carbon chain lengths will be compared. In the second, the time intervals between ketone pretreatment and administration of chloroform will be varied; in the third, dose-response relationships will be established. Finally, the ketone will be given repetitively. Minimally effective and non-effective potentiating doses will be determined.

Methods to be employed in assessing enphrotoxic effects include histological studies, the ability of renal cortical slices (rat) to take up an organic, acid p-amino hippurate (PAH), and an organic base tetraethylammonium (TEA), to convert lactate to carbon dioxide and to utilize oxygen.

The metabolism of choroform in suspensions of renal proximal tubules will also be studied in order to determine whether ketones potentiate $CHCI_3$ nephrotoxicity by increasing the conversion of $CHCI_3$ to reactive metabolites. Finally, the effects of ketones on the nephrotoxicity of mercuric chloride and potassium dichromate will be ascertained. If potentiation occurs, some mechanism other than enhanced biotransformation of the nephrotoxin must be involved. All drugs will be orally administered.

PROGRESS & ACCOMPLISHMENTS:

The investigators determined the ability of the identified ketones to potentiate chloroform induced kidney damage. Three of the five ketones tested were able to potentiate chloroform induced kidney damage. Currently, the investigators are liiking at the dose response relationship between ketones and the severity of damage produced by chloroform.

SIGNIFICANCE TO NIOSH:

This study will provide information in support of the hypothesis for predicting the ability of two classes of industrial solvents (ketones, and halogenated hydrocarbons) to interact and produce a potentiated toxic effect upon the kidney. In addition, the analysis of the mechanism by which ketones potentiate the nephrotoxicity of a representative halogenated hydrocarbon ($CHCl_3$) may permit the hypothesis to be expanded to include potentiating agents and nephrotoxins other than ketones and halogenated hydrocarbons which act upon the kidney in a similar fashion.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: April 1, 1979 - September 30, 1980

TITLE: Safe Decompression Schedules For Caisson Workers

PROJECT: 1 R01 OH00947-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Eric P. Kindwall, M.D.
Department of Hyperbaric
Medicine
St. Luke's Hospital
2900 W. Oklahoma Avenue
Milwaukee, WI 53215

GRANTEE INSTITUTION: Medical College of Wisconsin

OBJECTIVES:

- To develop new decompression tables for compressed air tunnel and caisson workers which reduce or eliminate the problem of dysbaric osteonecrosis
- To significantly lower the incidence of decompression sickness

METHODOLOGY:

Whole body nitrogen wash-out studies are being carried out to determine the amount of residual nitrogen present after decompression on the present tables is complete. During decompression, ultrasonic scanning of selected body tissues will be used to quantitate stationary bubble formation in the body during decompression. Modifications are being made in decompression profiles and length of steps as required to minimize gross bubble formation. This will be cross-checked with whole body nitrogen elimination measurements. After appropriate modification, a complete set of new decompression schedules will be generated for air decompression and also decompression using oxygen.

PROGRESS & ACCOMPLISHMENTS:

The ultrasonic tissue scanner has been set up and preliminary bubble imaging in tissues is now being carried out. The signal integration from the video output is currently being modified to produce a better graphic representation of bubble quantity. The preliminary new decompression tables have been completed and await full scale comparative testing.

SIGNIFICANCE TO NIOSH:

By using the above methods, it is highly likely that the new tables will be superior to the present ones. More positive assurance can be given that the dangers of aseptic necrosis have been lessened while minimizing the risk of decompression sickness or other complications in test subjects.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: February 1, 1980 - January 31, 1981

TITLE: Coal Dust Control by Condensation Enlargement

PROJECT: 5 R01 OH00822-02

PRINCIPAL INVESTIGATOR & ADDRESS: Franklin D. Schowengerdt, Ph.D.
Department of Physics
Golden, CO 80401

GRANTEE INSTITUTION: Colorado School of Mines

OBJECTIVES:

- To research and develop efforts aimed at applying the concept of condensation enlargement to the problem of controlling respirable coal dust in underground mines
- To design, construct and evaluate a laboratory prototype dust collection system
- To develop a dust collection system having the potential for greatly decreasing respirable dust concentrations in coal mines

METHODOLOGY:

This system involves the use of a parallel-plate condensation conditioner. Dust particles inside will nucleate water droplets and grow to collectable sizes, followed by a water spray. Design calculations are presented which indicate that the basic design capacity, dust load capacity, and water and energy consumption.

The design is based on data obtained previously on nucleation and water droplet growth on coal dust. The evaluation experiments will consist of measurements of output droplet sizes, coal dust transmission and water and energy consumption. During the evaluation, design parameters will be optimized for application to a full-scale model to be built and tested in the later phases of the program.

PROGRESS & ACCOMPLISHMENTS:

The results to date on this project indicate that most of the technical and engineering problems can be overcome. The base of background data on condensation enlargement that has been compiled in this laboratory indicate that there is no fundamental obstacle to developing an efficient dust removal system based on this concept which can eventually be placed in an operating underground mine.

SIGNIFICANCE TO NIOSH:

This research addresses a critical problem in underground mining and is likely to contribute to better dust suppression which would provide a healthier and safer working environment in mines.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: July 1, 1980 - June 30, 1981

Mining/Human/Cancer/
Epidemiology

TITLE: Epidemiologic Methods: U.S. Uranium Miners

PROJECT: 1 R01 OH00991-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Alice S. Whittemore, Ph.D.
Division of Epidemiology
Department of Family, Community, and Preventive Medicine
300 Pasteur Drive
Stanford, CA 94305

GRANTEE INSTITUTION:

Stanford University
School of Medicine

OBJECTIVES:

- To obtain information on the dose-response relationship for radon daughter exposure, particularly low level exposures
- To determine the nature and extent of interaction between radiation and smoking exposures in respiratory carcinogenesis
- To determine the presence or absence of a dose rate effect
- To determine the effect of age at start of radiation upon subsequent long cancer risk
- To determine the evolution of risk after termination of exposure
- To determine implications for risk due to occupational radiation exposures

METHODOLOGY:

Existing data on lung cancer mortality among approximately 4,000 U.S. uranium miners will undergo preliminary graphical analysis. Predictions of various multistage theories of cellular transformation and cancer growth will be compared to the observed lung cancer mortality rates. Parameters in the theories will be estimated by maximum likelihood, using a proportional hazards model. Goodness-of-fit will be tested. Implications for issues in human radiation will be discussed.

PROGRESS & ACCOMPLISHMENTS:

This is a new grant. Progress and accomplishments will be reported in the FY 81 grant report.

SIGNIFICANCE TO NIOSH:

The results from this investigation may lead to useful insights concerning the nature of lung cancer risk following radon daughter exposure.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date.

PERIOD COVERED: August 1, 1980 - July 31, 1981

TITLE: Damage - Risk Contours for Intermittent Noise Exposure

PROJECT: 2 R01 OH00350-07A1

PRINCIPAL INVESTIGATOR & ADDRESS:

Wallace Dixon Ward, Ph.D.
Hearing Research Laboratory
2630 University Avenue, S.E.
Minneapolis, MN 55414

GRANTEE INSTITUTION: University of Minnesota

OBJECTIVES:

- To analyze existing data on damage-risk limits for intermittent noise exposure
- To simplify the Committee on Hearing, Biomechanics and Bioacoustics (CHABA) contours

METHODOLOGY:

Human subjects (normal listeners) were exposed for eight hours to various patterns of interrupted noise. The temporary threshold shift (TTS) produced was measured at intervals from two minutes to 16 hours following exposure. Noise exposure parameters that were varied include octave-band frequency and level, rate of interruption, and noise burst duration. The effects of moderate noise during "quiet" periods are being studied, as well as the presence of pure-tone components in the noise, and irregular (multi-level) patterns. TTS based damage-risk criteria will be suggested. Equal-risk contours for intermittent noise will be constructed for each criterion.

PROGRESS & ACCOMPLISHMENTS:

SPL's that define effective quiet periods have been determined. The principle that the effective level of a fluctuating sound is given by its average spl (not average energy) has been confirmed. TTS at any given frequency was determined to be affected only by the noise components of one and a half octave or less. ingestion of alcohol was found to have a neligible effect on the growth of TTS or its recovery.

SIGNIFICANCE TO NIOSH:

This research should provide empirical data that will permit connection and simplification of the chaba contours, and the establishment of valid standards for tolerable intermittent exposures to noise.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Ward, W.D., The Total-Energy Concept as a Unifying Approach to the Prediction of Noise Trauma and its Application to Exposure Criteria. In Press
- Ward, W.D., Risks to Hearing: The Effect of Intermittent Exposure, International Symposium on Personal Hearing Prediction in Industry. J. Otolaryngology. In press

PERIOD COVERED: April 1, 1979 - December 31, 1980

TITLE: Animal Model to Study the Effects of Noise on Humans

PROJECT: 5 R01 OH00705-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Donald W. Neilsen, Ph.D.
2799 W. Grand Blvd.
Detroit, MI 48202

GRANTEE INSTITUTION: Henry Ford Hospital

OBJECTIVES:

- To identify an appropriate animal model used in studying the effects of long-term noise on the inner ear of humans
- To investigate the possibility of the squirrel monkey as the animal model by comparing the effects of a variety of noises on man and monkey

METHODOLOGY:

Twenty human subjects are being exposed to controlled noises of work-day durations where accurate measures of hearing sensitivity can be obtained. These controlled noise samples center octave bands of noise (OBN) at 500 Hz and 4 KHz and with pink noise. Records are maintained in the growth and recovery of temporary threshold shift (TTS) at these frequencies.

In addition, 12 squirrel monkeys are being used in behavioral and histological studies. The squirrel monkeys are trained to give behavioral measures of normal and shifted auditory thresholds. One ear of each animal is surgically altered to attenuate acoustic stimulation.

The animal will then be exposed to the same OBN as the human subjects. A small group of animals will be exposed to a higher intensity noise which causes permanent hearing damange. These animals' ears will be examined histologically by removing the bone with diamond burrs until only an eggshell thickness surrounds the cochlea and the vestibular system. The remainder can be decalcified in a few days. The cochleas are then impregnated with plastic and sectioned for light microscope.

PROGRESS & ACCOMPLISHMENTS:

Data have been obtained on 12 human subjects, each exposed twice to each of the five different noises for eight hours at each of two different sound pressure levels. Similar data have also been collected on six monkeys.

Work is proceeding on a technique for light and transmission electron microscope evaluation of cochleas in conjunction with decalcification of the temporal bone. These sections can be embedded in plastic slides for viewing with the light microscope, and desired areas then further sectioned for high magnification examination with the transmission electron microscope. Progress is being made toward the preservation of ultrastructure.

SIGNIFICANCE TO NIOSH:

There are few investigations on the appropriateness of any animal as a model for the effects of noise on hearing in the human. The results of the research will provide such data for the squirrel monkey. Once an appropriate animal model has been determined by these systematic investigations, the effects of noise exposure producing both TTS and permanent threshold shifts can properly be examined.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: March 1, 1979 - February 28, 1980

TITLE: Heat Strain: Biophysical and Physiological Evaluation

PROJECT: 5 RO1 OH00836-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Richard Gonzalez, Ph.D.
John B. Pierce Foundation
Laboratory
290 Congress Avenue
New Haven, CT 06519

GRANTEE INSTITUTION: Yale University of Medicine

OBJECTIVES:

- To validate a concept of physiological equivalence over a wide range of termal stresses
- To determine various physiological responses, such as changes in heart rate (HR) in esophageal temperature, total and regional sweating

METHODOLOGY:

The subjects in this study are young healthy persons over 18 years of age. Their physiological reactions will be observed in terms of a rational index of heat stress when exposed to various levels of temperatures and exercise. Subjects will be required to perform up to 4 hours of bicycle ergometer or treadmill exercise in ambient temperatures from 20 - 50° C at low and high humidities. Continuous recordings of skin temperature, internal temperature in the esophagus and local and total sweating will be made. Oxygen uptake and EKG will be monitored throughout an experiment. The effects of training, acclimation, and sex on the relationship of these various physiological factors to effective temperature will be reviewed.

PROGRESS & ACCOMPLISHMENTS:

Data indicate that body temperature responses are related to the fitness of the individual. Ratios were established for sensible to insensible heat exchange coupled to skin wettness levels. Adequate delineated of thermal limits evident by upward inflections of both heart rate and esophagecal temperatures.

Clad and unclad subjects in various temperature conditions according to the amount of clothing worn. Unclad subjects were studied under identical temperature conditions. It was found that females of average fitness were less tolerant of dry heat stress compared to males but that differences vanished in fit females.

SIGNIFICANCE TO NIOSH:

This research incorporates the effects of other physiological factors such as cardiac output, stroke volume, study of hydration and type of work as a function of rational index Effective Temperature (ET). The procedures used in the assessment of multiple physical and physiological factors for occupational heat stress may offer rational approach towards characterization of heat tolerance in the workplace.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Gonzalez, R.R.: 1980: Exercise Physiology and Sensory Responses, Bioengineering, Thermal Physiology and Comfort, K. Cena and J.A. Clark (eds). Wroclaw Technical University Press, Wroclaw, Poland, in press.
- Gonzalez, R.R.: 1979: Role of Natural Acclimatization (cold and heat) and Temperature: Effect on Health and Acceptability in a Built Environment, Indoor Climate, Banish Building Institute Press, pp 737-751.

PERIOD COVERED: April 1, 1979 - March 31, 1980

TITLE: A Symposium: Effects of Noise and Hearing

PROJECT: 1 R13 0H00848-01

PRINICIPAL INVESTIGATOR & ADDRESS:

Donald Henderson, Ph.D.
1966 Inwood Rd.
Dallas, TX 75235

GRANTEE INSTITUTION:

University of Texas
Collier Center for
Communicative Disorders

OBJECTIVES:

- To organize and assemble an international symposium on noise-induced problems presented by research audiologists

METHODOLOGY:

The three day conference was patterned after a conference held in 1975, at which audiological investigators presented their latest findings. The conference expanded the scope and context of the effects of noise and hearing. It covered morphological, biochemical, electrophysiological and behavioral mechanisms. Special emphasis was placed on impulse, impact noises, and the problem of searching for more reliable indicators of cochlear damage. All papers presented in the symposium will be compiled into a final publication.

PROGRESS & ACCOMPLISHMENTS:

The symposium was held in June, 1980 and the results are being prepared for publication.

SIGNIFICANCE TO NIOSH:

The conference provided an opportunity for noted investigators to present and discuss the state of the art in noise-induced hearing problems. The papers submitted for final publication will serve as an important resource on this topic.

PUBLICATIONS RESULTING FROM THIS GRANT:

Symposium Proceeding. In press.

PERIOD COVERED: September 1, 1979 - August 31, 1980

Physical Agents/Control Technology/Human

TITLE: Thermoregulatory Response of Women

PROJECT: 5 R01 OH00858-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Barbara Drinkwater, Ph.D.
Institute of Environmental Stress
Santa Barbara, CA 93106

GRANTEE INSTITUTION: University of California

OBJECTIVE:

- To evaluate the ability of the thermoregulatory and cardiovascular system to integrate the physiological demands of intermittent exposure to heat and work

METHODOLOGY:

The subjects will work either continuously or intermittently in environments ranging from 20-30° work CET at work loads approximately 30% and 50% of their maximal aerobic power (Vo_2 max). During intermittent work the subject will rest in a cool environment. The total energy expenditure during the 120-minute intermittent and continous work sessions will be equal. At each CET there will be two ambient conditions, one with a high radiant load and a low vapor pressure and the other with a low radiant load and a high vapor pressure. Physiological variables considered include metabolic, temperature, sweat and cardiovascular responses.

PROGRESS & ACCOMPLISHMENTS:

Data from eight matched pairs for steady state and intermittent work under high and low radiant conditions indicate that: 1) under both high and low radiant condictions, the women can complete equivalent work with less physiological strain under the intermittent protocol, 2) there is a suggestion that the high radiant conditions results in a greater stress, particularly on the cardiac and sweat responses, 3) the fine core temperature for the women after two hours of work are within $\pm$ 0.1°C of the values reported for male soldiers at the end of one hour of work at similar CET's. Exercising at a higher work rate, the women were able to accomplish as much absolute work in the intermittent protocol and also benefitted physiologically from a rest in a cooler environment.

SIGNIFICANCE TO NIOSH:

The results from this study may provide information needed in setting realistic environmental standards for hot industries.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: April 1, 1979 - March 31, 1980

TITLE: Physiological Responses to Exposures to Intermittent Heat

PROJECT: 1 R01 OH00874-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Stephen A. Konz, Ph.D.
Institute for Environmental
Research
Manhattan, KS 66506

GRANTEE INSTITUTION: Kansas State University

OBJECTIVES:

- To develop rational, dependable guidelines for permitted exposure to intermittent heat stress for clothed workers
- To determine the clothing worn in industrial heat stress environments
- To determine the insulation value of this clothing
- To determine the physiological responses of acclimatized and unacclimated clothed individuals exposed over an eight hour period to various work-rest schedules of intermittent heat stress
- To develop guidelines for workers in intermittent heat stress

METHODOLOGY:

This investigation consists of five phases: clothing worn in the field, insulation values, physiological responses, model validation, and intermittent heat stress guidelines. In Phase 1, typical clothing ensembles worn in heat stress of at least 25 organizations will be determined. In Phase 2, using an electrically heated copper mannequin, investigators will determine insulation values (clo) of typical ensembles from Phase 1.

In Phase 3, physiological responses will be measured on 12 acclimatized subjects at four temperature levels, three work-rest cycles, three clothing levels and two recovery levels. Each session will last 10.5 hours (pretest, heat, post-test sessions with time for subjects to have coffee and lunch breaks in controlled environments). Heart rate, skin temperature, rectal temperature and clothing surface temperatures will be recorded automatically on tape every five minutes. Weight loss will be recorded every 60 minutes.

In Phase 4, from previous data and from Phase 3, investigators will validate the biophysical 25 node human thermoregulatory model for clothed exercising individuals exposed to intermittent heat stress. In Phase 5, from the experimental data and computer simulations using the model, guidelines will be developed giving permitted exposure to intermittent heat stress for clothed workers.

PROGRESS & ACCOMPLISHMENTS:

Selections were made of three representative clothing ensembles for the human subjects to wear in the chamber tests planned for Phase 3 of the project. The selection was based on design features, fabric type, insulative values, and frequency of use in hot industrial environments. The garments were purchased from the manufacturers through a textile services firm which laundered the garments twice prior to subject use.

To complete the objectives of Phase 2, measurements will be obtained of the permeability index (i_m) of the clothing using the "sweating" copper mannequin. The ratio of i_m/clo is a better indicator of the potential for heat loss via radiation, convection, and evaporation than the insulative value alone.

To prepare for the Phase 3 experiment, a pilot experiment with four subjects was conducted. The subjects stepped (Master's Step Test) at a metabolic rate averaging 325 W for six hours per day for each of the eight days. The subjects wore the standard KSU ensemble (long sleeve shirt and trousers). This experiment provided good data and permitted the fine tuning of procedures.

SIGNIFICANCE TO NIOSH:

Results from the experiment, used in conjunction with computer simulation and literature review, may be used to propose rational, defendable guidelines for intermittent exposure to heat stress.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 28, 1979 - August 31, 1980

TITLE: Attenuation Characteristics of Hearing Protectors

PROJECT: 1 R01 OH00895-01A1

PRINCIPAL INVESTIGATOR & ADDRESS:

Larry E. Humes, Ph.D.
Division of Hearing and
Speech Sciences
Nashville, TN 37232

GRANTEE INSTITUTION: Vanderbilt University

OBJECTIVES:

- To examine the attenuation characteristics of hearing protectors at low and high sound intensities
- To evaluate the stability of hearing protectors

METHODOLOGY:

Two new methods of assessing hearing protectors in low and high levels of noise will be examined on human subjects. These methods are cross-modality matching and a masked bone-conduction threshold procedure. In the latter method, fixed frequency bone-conduction thresholds for pulsed pure tones are determined using a Bekesy tracking technique.

Earplugs will be evaluated for hearing protector stability.

PROGRESS & ACCOMPLISHMENTS:

Preliminary set up and calibration of laboratory equipment is being completed. Preliminary data regarding procedural modifications have been collected.

SIGNIFICANCE TO NIOSH:

Improving the existing standard for the measurement of real-ear attenuation provided by hearing protectors will increase the effectiveness of this hearing conservation strategy.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: May 1, 1980 - April 30, 1981

Physical Agents/Human/
Clinical/In Vivo

TITLE: Physiological Adaptation of Women to Heat Stress

PROJECT: 5 RO1 OH00896-07

PRINCIPAL INVESTIGATOR & ADDRESS:

Barbara Drinkwater, Ph.D.
Institute of Environmental
Stress
Santa Barbara, CA 93106

GRANTEE INSTITUTION: University of California

OBJECTIVES:

- To examine the mechanisms involved in age-related differences in the thermo regulatory system of females
- To investigate the role of central and peripheral mechanisms in the sweating responses of women of all ages
- To examine the relationship of cardio vascular endurance (VO_2 max) to heat tolerance of women

METHODOLOGY:

To accomplish the objectives in this investigation, a basic experimental design will be adopted that deals with age, environment, workload, and time. Subjects will undergo preliminary screening that consists of informal consent, and a physical examination including a 12 lead ECG and pulmonary function tests. If the ECG is within normal limits, the subjects's maximum oxygen consumption will then be determined. Body density will be determined by underwater weighing and blood volume will be measured.

PROGRESS & ACCOMPLISHMENTS:

A computer assisted device for measurement of peripheral bloodflow has been developed, which permits automatic inflation of the pressure cuffs at programmed intervals, transmission of resistance changes in the Whitney mercury-in-silastic strain gauge to the PDP 11/60 computer, and real-time calculation of blood flow.

SIGNIFICANCE TO NIOSH:

The results of such studies will provide us with a better understanding of how the female responds to the challenge of hot environments and provides insight into some unanswered questions in the area of thermoregulation in general.

Specifically, these studies will examine how females respond to heat stress, pointing out the minimal effect of the menstrual cycle and describing the role of cardiovascular endurance during acute exposure to heat stress.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: May 1, 1979 - April 30, 1980

TITLE: Textile Industry Noise Technology Research Program

PROJECT: 1 R01 OH00933-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Paul Emerson
PO Box 5006
Raleigh, NC 27650

GRANTEE INSTITUTION:

North Carolina State
University at Raleigh

OBJECTIVES:

- To expand technical information available to the textile industry for use in determining and achieving favorable reductions of employee exposure to occupational noise

METHODOLOGY:

Specific emphasis will be placed on more sophisticated noise source diagnostic techniques. This will be achieved through the use of a computer that has multi-channel signal processing capabilities to compute statistical series data and to obtain field data for machine categories not available in laboratories. In addition, studies on weaving shuttleless looms, weaving-fly shuttle looms, ring spinning, winding, twisting, texturing, other machinery, and machinery noise specifications will be continued to provide more economic and efficient means of reducing noise in the textile industry.

PROGRESS & ACCOMPLISHMENTS:

A new mini-computer is being utilized to perform coherence and correlation studies. Air-Jet loom noise is under investigation through studies on an INVESTA-P-125 Air-Jet loom. A fly-shuttle loom has been set-up in an anechoic chamber for fundamental analysis of impact noise, utilizing a telemetry system to measure shuttle and acceleration. Finite element analysis is being used to develop advanced spindle design to minimize spinning noise. Texturing noise studies include development of test equipment and noise source identification studies which are in progress.

SIGNIFICANCE TO NIOSH:

This research is likely to provide new information for the textile industry on advanced noise control activity. The results will be shared with industrial organizations through conferences and cooperative projects, leading to greater understanding and to potentially viable solutions of noise problems in working environments.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Cooke, J.A. and Baiely, J.R.:1979: Analysis of DSL-Rapier Loom Noise Using Digital Signal Processing, Measurements for Industrial Noise Control, issued by American Society of Mechanical Engineers.

PERIOD COVERED: December 1, 1979 - November 30, 1980

TITLE: Midfrequency Dysfunction in Noise-Exposed Persons

PROJECT: 1 R01 OH00972-01

PRINCIPAL INVESTIGATOR & ADDRESS:
Larry Humes, Ph.D.
Division of Hearing and
Speech Sciences
Nashville, TN 37232

GRANTEE INSTITUTION: Vanderbilt University

OBJECTIVES:

- To examine in detail the possibility that subtle midfrequency hearing dysfunction which goes undetected by pure tone audiometry may exist in noise-exposed listeners
- To evaluate midfrequency auditory function in a large sample of noise-exposed listeners
- To examine the relationship between the extent of dysfunction and communicative breakdown

METHODOLOGY:

Psychophysical tuning curves, pure-tone masking patterns, pure-tone unmasking, and masked speech reception threshold are methods which are being used to assess midfrequency dysfunction. In addition, two methods will be used to assess communication breakdown: the California Consonant Test and the Hearing Performance Inventory. Proper control groups will be tested with discriminating psychol-physical measures and these measures will be correlated with appropriate measures of communication ability, i.e., the California Consonant Test and the Hearing Performance Inventory.

PROGRESS & ACCOMPLISHMENTS:

Preliminary setup and calibration of laboratory equipment is being completed. Preliminary data regarding procedural modifications have been collected.

SIGNIFICANCE TO NIOSH:

The project will provide a perspective on the prevalence of the subtle dysfunction from noise exposure at frequencies below 2 kHz and how important this dysfunction is in detecting realistic speech perception.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: May 1, 1980 - April 30, 1981

TITLE: Dexterity of Females in Cold Environment

PROJECT: 1 R01 OH01029-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Michael Riley, Ph.D.
175 Nebraska Hall
Dept. of Industrial Engineering
Lincoln, NE 68588

GRANTEE INSTITUTION: University of Nebraska

OBJECTIVES:

- To determine if a decrement in manual dexterity of females occurs with a reduction in environmental temperature
- To quantify the amount of change in dexterity due to a change in environmental temperature
- To identify the type of manual activity that is most significantly influenced by environmental temperature
- To obtain a representive sample of persons whose normal activities are dependent in dexterity in order that performance and working guidelines can be proposed

METHODOLOGY:

This study is examining and comparing a minimum of 30 female and 30 male subjects in a variety of manipulative tests. A regression model will be developed to predict dexterity at different temperatures. Performance will be correlated with other measures of response such as heart rate, hand and skin temperature. Temperatures at which alternations in performance become evident will be identified. The selected testing site will be standardized to contain constant humidity, air velocity, air elimination and noise. Selected college students, homemakers, and industrial workers are being trained in the proposed dexterity tasks. Changes in dexterity as a function of temperature for females will be documented.

SIGNIFICANCE TO NIOSH:

This study will further the understanding of female workers' manual dexterity capabilities at reduced temperatures.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: April 1, 1979 - September 30, 1980

TITLE: The Effects of Impulse Noise on the Auditory System

PROJECT: 1 R01 OH1152-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Donald Henderson, Ph.D.
Callier Center
1966 Inwood
Dallas, TX 75235

GRANTEE INSTITUTION:

The University of Texas Dallas
Callier Center for
Communication Disorders

OBJECTIVE:

- To establish the relationship between the physical factors of impulse noise and their effects upon anatomical, physiological and behavioral aspects of the ear

METHODOLOGY:

Animals were exposed to impact noise of 120 dB and 106 dB levels at the rate of one second for 10 days, and exposed to 101 dB impulse noise eight hours per day for five days. Correlations were obtained between behavioral, physiological, and anatomical changes in the cochlea and VIII nerve associated with chinchillas that have either low-level, high frequency permanent threshold shift(PTS) or broad 40-50 dB asymptotic threshold shift (ATS) from 250 to 12,000 Hz.

An alternative was to devise a technique which easily and rapidly assessed the biochemical integrity of the cochlear sensory cells, that is, to develop a histochemical cochleaogram. Methods were devised for generating impulses over periods as long as three months continously operating at a one impulse per second rate.

A battery of psychophysical tests was developed to more accurately and comprehensively assess the behavioral and anatomical impairment from noise damage. One approach was to measure auditory temporal processing as well as quick threshold. The next stage of these experiments consisted of measurement of detection with various levels of hearing loss and cochlear damage.

An experimentally based compromise procedure was developed whereby AER thresholds can be collapsed with behavioral thresholds, thereby increasing the effective sample size.

PROGRESS & ACCOMPLISHMENTS:

It was found that the level of ATS as a function of stimulus level grows faster for impulse noise than continous noise, in fact, at a rate about double that of continous noise.

An electromechanical source was developed and has proven to be a reliable means for generating impulses over periods as long as three months continous operation at the one impulse per second rate. Another alternative being explored is a digital system that would sample an impulse and then play it back through an A/D conversion.

The results of the behavioral test battery for the 10KHz are:

- Over a 30 dB range (i.e., 8 dB to 28 dB spectral level) the gap duration threshold for the five animals was approximately 3 m Sec. and,
- When the intensity level was decreased to - 2 and -12 dB SPL the gap thresholds increased to about 4 and 6 m Sec respectively. These results are in close agreement with human performance.

In the average evoked response and behavioral approaches before and after noise exposure, all three animals, at each time of measurement, showed exceptionally good agreement between the two indices of hearing threshold.

SIGNIFICANCE TO NIOSH:

This study is producing indications of the risks posed by impulse noise. The noise exposure received by the experimental animals is similar to that which human workers may be receiving.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Henderson, D., Hamernik, R.P., Hynson, K.: Impulse Noise Induced Hearing Loss From Simulated Work-Week Exposures; J. Acoust. Soc. Am. In press.
- Blakeslee, E.A., Hynson, K., Hamernik, R.P., Henderson, D.: 1977: "Interaction of Spectrally Mismatched Continuous and Impulse Noise Exposures in the Chinchilla," J. Acoust. Soc. Am.
- Hamernik, R.P., Henderson, D., Coling, D.: "Interaction of Sinusoidal Vibration and Impulse Noise: Auditory Effects," J. Acoust. Soc. Am.
- Salvi, R., Henderson, D., Hamernik, R.P.:1979: "Single Auditory Nerve Fiber and Action Potential Latencies in Normal and Noise-Treated Chinchillas." Spring meeting, Assoc. for Research in Otolaryngology.
- Giraudi, D.M., Salvi, R.J., Henderson, D., Hamernik, R.P., Blakeslee, E.A.:1979: "Detection of Silent Intervals in Noise by Chinchillas," Spring Meeting, Assoc. for Research in Otolaryngology.
- Hamernik, R.P., and Henderson and Coling:1980: Interaction of Whole Body Vibration and Impulse Noise. J. of Acoutical Society of America, v. 67, p. 28.

- Hamernik, R.P., Henderson, D., Salvi, R.J.: The Influence of Vibration on Asymptotic Threshold Shift Produce by Threshold Noise, Audiology, v. 19. In press.

- Slepecky, N., Hamernik R.P., Henderson, D.:1980: A Reexamination of a Hair Cell Organalle in the Cuticular Plate Region and its Possible Relation to Active Process in the Cochlea. Hearing Research, v. 2, p. 413.

PERIOD COVERED: May 1, 1979 - April 30, 1980

Protective Equipment/
Human/In Vivo

TITLE: Respiratory Stress and Occupational Respirator Wear

PROJECT: 5 R01 OH00735-03

PRINCIPAL INVESTIGATOR & ADDRESS: Arthur T. Johnson, Ph.D.
Sports Medical & Physical
Fitness Center
College Park, MD 20742

GRANTEE INSTITUTION: University of Maryland

OBJECTIVES:

- To investigate characteristics of persons who experience severe respiratory difficulty while working
- To demonstrate that as exhalation time decreases, airways resistance increase
- To correlate minimum exhalation time through modelling

METHODOLOGY:

Ten normal subjects and 10 subjects with respiratory abnormalities were used to measure airways resistance with the Airflow Perturbation Device (APD) and with Boyd's plethysmograph. A direct comparison between the new instrument and the standard technique was analyzed. The APD, unlike the Boyd plethysmorgraph, was able to determine resistance within a single breath.

Twenty healthy subjects young and old, male and female participated in an exercise study to determine correlates of minimum exhalation time. Exhalation time and airways resistance were measured with the APD, while oxygen consumption, minute volume, and respiratory quotient were obtained with a metabolic measurement chart. All subjects underwent a complete battery of pulmonary function tests.

Correlation and transgeneration of data was performed to determine if minimum exhalation time could be predicted from age, sex, physical condition, or sedimentary pulmonary function test results. A relationship between airways resistance and exhalation time was investigated. The study examined the effects of minimum exhalation time on the anaerobic threshold during exercise.

PROGRESS & ACCOMPLISHMENTS:

Major findings include: APD underestimates airways resistance; no direct comparison between methods of airways resistance measurements can be easily made on animals. The APD causes no pressure perturbations at points more distal than the alveoli.

The APD must be modified to include a screen resistance to be varied as measurement sensitivity dictates. Phase angle between mouth pressure and flow may be useful to estimate compliance. APD screen rotation rate should be faster when the subject breathes faster.

SIGNIFICANCE TO NIOSH:

The APD may become a useful worker surveillance tool.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Johnson, A.T., and NcCuen, R.H.:1980: A Comparative Model Study of Respiratory Period Prediction on Men Exercising While Wearing Masks. IEEE. on Biomedical Engineering, v. BME-27, p. 430-439.

PERIOD COVERED: September 1, 1979 - August 31, 1980

TITLE: Fracture Resistance of Ophthalmic Lens/Frame Systems

PROJECT: 5 R01 OH00766-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Werner Goldsmith, Ph.D.
Department of Mechanical
Engineering
Berkeley, CA 94720

GRANTEE INSTITUTION: University of California

OBJECTIVE:

- To provide definitive guidelines for the design and construction of optimally safe lens frames systems with respect to specified impacts, achieved by proper selection of materials, dimensions, fabrication techniques and geometrical parameters

METHODOLOGY:

The testing phase consist of projection of strikers into a variety of lens/frame combinations at speeds similar to those found in practice, such as stones thrown up by vehicles or metal cuttings separating from work pieces. The corresponding analytical approaches utilize the finite element technique for the determination of the mechanical response parameters resulting from the controlled loadings. The effects of various mounting methods, including bevel configurations and eyewire grooving, on the frangibility of the systems is being investigated. The correlation of data and analytical prediction of displacement and stresses from such investigations permit an assessment of the validity of the model, and allows the use of the latter as a design tool to permit the construction of safer, and perhaps less expensive, lens/frame combinations.

PROGRESS & ACCOMPLISHMENTS:

A square mesh was initially used in the application of the finite element method for the problem of impact on an ophthalmic lens/frame system. The program was reconstructed from earlier efforts and eventually yielded results on the digital computer. However, comparison of these predictions with corresponding test data indicated that the mesh utilized was not nearly accurate enough for the purposes intended. Consequently, current efforts involve the development of an entirely new mesh system for the program.

Lenses ranging from +4 to -4 diopters, both supported on the FDA test stand and inserted in a frame placed over a humanoid head are being subjected to impacts of increasing severity up to fracture. Strains in the entire system and forces transmitted to the head are measured. The effect of eyewire tension and prestress in the lenses on impact resistance is being investigated.

SIGNIFICANCE TO NIOSH:

The results of this effort should provide safer eyeglasses under a variety of accidental impact situations.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 28, 1979 - August 31, 1980

Protective Equipment/Asbestos
and Asbestos Substitutes/
Testing

TITLE: Asbestos Substitute Fabrics for Safety Clothing

PROJECT: 1 R01 OH00910-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Roger L. Barker, Ph.D.
Department of Design &
Environmental Analysis
Ithaca, NY 14853

GRANTEE INSTITUTION: Cornell University

OBJECTIVES:

- To selectively survey industries where asbestos or heat-resistant fabrics are used
- To identify heat resistant fabrics other than asbestos
- To evaluate the thermal response of various fabrics
- To evaluate the textile properties of various fabrics
- To competitively rank the fabrics

METHODOLOGY:

A survey was conducted of the industrial users of asbestos and heat-resistant fabrics. A literature review was conducted to define the needs and uses of asbestos in industrial high-temperature fabrics and safety devices. Safety engineers were interviewed for information concerning the uses and requirements for "asbestos-like" heat resistant fabrics. Worksites were visited to observe the use of asbestos in heat-resistant garments.

A survey was conducted to identify the producers of heat-resistant fabrics. Sample fabrics were obtained from various commercial sources. Test procedures including heat transmission and linear shrinkage were used to measure the fire athermancy of the fabrics. A test was used to measure the heat transmitted by the fabrics when in direct contact with a hot material.

Heat transmission and fire athermancy results were analyzed using a computer. Various tests were conducted to evaluate the textile properties of the fabrics, which included fabric construction and composition, strength and durability, permeability and flexibility. Laundering test were conducted to determine the ability of the test fabrics to withstand normal cleaning or refurbishing without losing the original textile properties.

The fabric samples were ranked in order of performance and rated based on potential for effective thermal protection and potential usefulness in an industrial environment.

PROGRESS & ACCOMPLISHMENTS:

The following progress and accomplishments were conducted during the progress period:

- Completed literature review
- Surveyed the following:
  - Industrial engineers/professionals
  - Manufacturers of protective clothing
  - Producers of heat-resistant fabrics
- Completed analysis on the survey data
- Completed tests and evaluation of fabrics
- Designed a testing apparatus that simulated radiant/convection heat hazards
- Determined the ability to predict serviceability of heat resistant fabrics

SIGNIFICANCE TO NIOSH:

The intent of this project was to identify high temperature fabrics other than asbestos which will provide effective means of protecting the industrial worker against heat hazards. The study may contribute to the development of information and resources to be used in the design of superior thermal protective clothing for industrial applications.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 28, 1980 - August 31, 1981

Radiation/Cancer/
Epidemiology/Human

TITLE: Occupational Health Risks of workers in Atomic Plants

PROJECT: 1 R01 OH00929-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Thomas F. Mancuso, M.D., M.P.H.
130 Desoto Street
Pittsburgh, PA 15261

GRANTEE INSTITUTION: University of Pittsburgh

OBJECTIVES:

- To conduct a prospective epidemiological mortality study, retrospective in time from 1944, of cohorts of employees hired in successive years
- To determine the occupational risks among workers in an atomic energy facility
- To study the long-term delayed biological effects of low-level ionizing radiation in a normal adult industrial population, that has been chronically exposed to fractionated doses of low-level ionizing radiation over a span of years

METHODOLOGY:

This epidemiological study consists of the long-term effects of chronic exposure to low-level ionizing radiation in normal adult industrial populations. It involves workers employed since 1944 at Hanford Works Atomic Plant, (Richland, WA), who have been exposed to fractionated doses of low-level ionizing radiation over a span of years. These workers have had their occupational radiation exposure measured and recorded on a uniform basis during their period of employment. The total study involves approximately 35,000 workers as well as a matched control population. Successive cohort analyses of employee populations, with simultaneous control of employment exposures, employment patterns, occupations and external and internal radiation measurements are being carried out. The study involves extensive occupational analysis required to identify whether any occupational group is at higher mortality risk for specific causes of death as compared to other occupational population groups and what factors may be associated with such findings. The data collected and analyzed includes both radiological and non-radiological occupational exposures.

Vital statistics and cause of death will be obtained from the Social Security Administration and State mortality records. The analytical method involves division of the cohort into groups according to sex, 2 levels; age at hire 5, levels; work cohort, 4 levels; length of employment, 3 levels; and internal radiation, 4 levels. Within each of these groups, a life table was constructed to provide a follow-up mean cumulative radiation dose received by those dying of cancer during the year as compared with the mean cumulative radiation dose of cancer deaths and that of survivors over all years of follow-up. A summary statistic was obtained for each of the control groups representing the deviation between mean cumulative radiation dose of cancer deaths and that of survivors overall years of follow-up. Finally, these deviations will be aggrevated over the control groups and a standardized statistic will be constructed to test the null hypothesis of no radiation effects. In addition, some models of dose-response were constructed and the method of maximum likelihood was used to estimate parameters such as doubling dose, latent period, and age sensitivity along with confidence intervals for these parameters.

PROGRESS & ACCOMPLISHMENTS:

The processing of Hanford employees and controls has been sent to the Social Security Administration (SSA) in the various states identified by SSA. Regression models have been developed for the correlation analysis of cancer risk with radiation for the Hanford data.

Bioassay data have been replaced by an index of the hazards of the work performed by each worker. Results show that the "healthy worker effect" has been brought under control by an index which is independent of the radiation records and that there has been firm rejection of the null hypothesis by the cancers of radiosensitive tissues.

SIGNIFICANCE TO NIOSH:

The significance of the project is as follows: 1) it relates to the identification of the extent of the contribution of low-level ionizing radiation in the development of cancer; 2) it identifies methods for the control of exposure to ionizing radiation as reflected in standards for the industrial population, the population around nuclear facilities and the general population; and 3) it aid in the establishment of scientific resources for the study of a normal population in which observations of radiation effects may be continued for many years.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Kneale, G.W., Mancuso, T.F., Stewart, A.M.: Hanford Radiation Study III, a Cohort Study of the Cancer Risks From Radiation to Workers at Hanford (1944-1977 deaths) by the Method of Regression Models in Life-Tables, The British Journal of Industrial Medicine. In press.
- Stewart, A.M., Kneale, G.W., and Mancuso, T.F.:1980: The Hanford Data--A Reply to Recent Criticisms, Ambio, vol.9, No. 2. April, 1980.

PERIOD COVERED: August 1, 1979 - July 31, 1980

NIOSH REPRODUCTIVE EFFECTS GRANT PROGRAM

On June 30, 1980 NIOSH initiated the active solicitation of research and demonstration grants in the area of reproductive effects due to workplace hazards. The standard National Institutes of Health (NIH) application and review procedures are followed in all NIOSH grants programs.

BACKGROUND

A major NIOSH responsibility is to conduct research necessary to ensure, insofar as possible, that no worker will suffer diminished health, reduced functional capacity, or decreased life expectancy as a result of his or her work experience. As a part of this responsibility NIOSH is concerned with discovering the identity and, if possible, the prevalence of physical and chemical hazards to which male and female workers who are exposed that might affect the development of their unborn children. While a relatively few chemical and physical agents are generally accepted as proven mutagens, teratogens, or carcinogens in humans, over a thousand agents are reported to have these effects in animals. Furthermore, many of these agents are reported to be mutagenic in biological test systems and thus, must be suspected as capable of causing reproductive effects in humans.

Over the past several decades there has been a threefold increase in the number of women employed in the U.S. workforce. During this period women have been employed in more hazardous occupations including those traditionally restricted to men. In recent years an increasing number of pregnant women have remained on the job until near the end of pregnancy. Thus, many more women and their unborn children are being exposed to chemical, physical, and psychological hazards of the workplace. Despite this fact, very little is known about the impact of such exposures on fetal wastage, growth and development.

Because of the unique role of women in the reproductive process, exposure to chemical and physical hazards has targetted attention on the risks to the offspring of maternal exposure. In so doing, we tend to forget that the working male exposed to mutagenic agents also places the health of his offspring at risk.

Other areas of concern are:

- Recognition of the potential that exists for harm to the germ cells of parents of both sexes signals a need to investigate the possibility that occupational hazards might affect the fertility of both men and women;
- The realization that significant quantities of industrial materials may be brought home in clothing resulting in the potential exposure of non-working pregnant women, makes studies of teratogenicity of agents to which male workers are exposed as important as studies of infertility and mutagenicity; and

- The possibility that childhood cancers may be related to prenatal environmental exposures.

NIOSH is offering both a challenge and an opportunity to talented researchers interested in the study of reproductive effects from occupational exposures.

AREAS OF RESEARCH INTEREST

The goal of this program is to stimulate and encourage high quality research and demonstration grants in several important areas of research. These areas are not mutually exclusive. It is anticipated that a given research study may cut across several areas. Included under each listed area are examples of the types of studies which would be of interest to NIOSH. They are not meant to be restrictive and are cited for illustrative purposes only.

A. EPIDEMIOLOGY AND BIOMETRY: Projects which consider the epidemiology of reproductive effects, including altered fertility, spontaneous abortions, fetal deaths, genetic diseases and disorders and childhood cancer, resulting from chemical and physical occupational hazards. Of particular interest are studies where dose-effect relationships are identified or determined. NIOSH is interested in epidemiological research using a vareity of methods or approaches. Such methods include those which generate hypotheses and typically used registries, medical records or statistics as the primary data source and those methods which tend to confirm hypotheses by demonstrating dose-effect relationship or the prevention of an effect by interruption of exposure. Specific examples of epidemiology studies include:

- Studies which identify groups of workers with abnormal reproductive experience and determine probable cause.
- Studies to determine whether an incidence of infertility, spontaneous abortion, or fetal mortality in the reproductive experience of a specific group of workers and/or spouses is abnormal.
- Studies to assess the parental employment relatedness of cancer in childhood.
- Studies on known reproductive hazards to evaluate and compare methodologies and to determine association between endpoints of the methodologies.

B. TOXICOLOGY: Projects to identify reproductive (mutagenic, teratogenic, etc.) hazards of chemcials to workers and to provide an early warning of the possible deleterious effects. Specific examples include:

- Research which develop test systems to detect mutagenic activity of air particulates, chemical mixtures or complexes found in the workplace.
- Projects which study the possible synergistic effect of mutagenic and teratogenic chemicals produced in workplaces.

- Research to validate human cell mutagenic assay systems.

- Studies which evaluate the usefulness of body fluid analysis and cytogenic assay systems for the assessment of the mutagenic hazard of chemicals to workers.

C. EXPERIMENTAL LABORATORY INVESTIGATIONS: Projects to elucidate the biochemical and physiological mechanisms of activity and nature of reproductive hazards in the workplace. Examples include:

- Studies to develop and validate screening systems based upon biochemical, enzymatic, or hormonal components of body fluids (e.g., blood, urine, semen) that can be used as reliable indices of the functional state of the reproductive system.

- Investigations to develop, improve, or validate short-term or *in vitro* methods for teratogenesis testing.

- Studies of mechanisms of teratogenesis, with the goal to improve the ability to predict relative teratogenic potential of chemically related compounds or to make inter-species extrapolations of teratogenesis data.

- Research on the mechanisms by which abnormalities are induced in sperm head morphology and the implications of morphological changes as indicators of induced mutations or of impaired reproductive capacity.

D. CONTROL TECHNOLOGY: Projects to develop new and improved methods or equipment to prevent reproductive effects from occupational hazards

- Studies which identify workers potentially or actually exposed to reproductive hazards and design new or improved controls for the hazards.

- Research which adapts existing methods, as well as develop new methods of monitoring and controlling reproductive hazards in the workplace.

- Research which seeks to use innovative approaches, such as alternative materials, engineering controls, process modification and protective equipment to prevent known or suspected reproductive problems.

Reproductive Effects/
Toxicology/Clinical Studies/
In Vivo/In Vitro/Animal

TITLE: Biological Effects of Nitrous Oxide as Used in Dentistry

PROJECT: 5 R01 OH00742-03

PRINCIPAL INVESTIGATOR & ADDRESS:	Carl A. Verrusio, Ph.D. 211 East Chicago Avenue Chicago, IL 60611
GRANTEE INSTITUTION:	American Dental Association Health Foundation

OBJECTIVES:

- To investigate the toxic effects, if any, of nitrous oxide at low levels and delineate the biochemical mechanisms of this toxicity
- To determine if chronic exposure to low levels of nitrous oxide is teratogenic and/or mutagenic in rats and mice

METHODOLOGY:

Pregnant mice and rats were exposed to chronic low concentrations of nitrous oxide for various periods of time during gestation. The mice and rats were then sacrificed to determine the rate of fetal death and the incidence of congenital malformations in their offspring.

Male mice and rats which were exposed to nitrous oxide for prolonged periods of time were mated with unexposed females to assess the mutagenic potential of nitrous oxide on sperm. The male reproductive performance, after several months of exposure, was then compared to the reproductive performance of a control group. Histological and electron microscopic studies of the testes were completed to determine changes and how they correlate with the reproductive records.

Toxic effects were studied in vivo and in vitro. Adult male and female mice were exposed to various low levels of nitrous oxide for one to twelve weeks in the in vivo portion of the study. The animals were sacrificed and their tissues studied as follows:

- Liver, lungs, kidneys and testes were sectioned for histopathology, and blood samples were collected for serum levels of glutamic pyruvic transaminase as an indicator of hepatic toxicity
- Microsomes from liver, lung, kidney and testes were prepared and various drug-metabolizing enzyme levels and activities determined, and

- Mice and rats from the teratogenic and mutagenic studies were investigated to assess the effects of nitrous oxide on drug-metabolizing enzymes in maternal and fetal tissues

The same determinations were made in the in vitro experiments on liver, lung, kidney and testicular tissue taken from unexposed animals and incubated with various mixtures of nitrous oxide and air (or oxygen and nitrogen) under controlled conditions.

PROGRESS & ACCOMPLISHMENTS:

Exposure of male rats to 20 percent nitrous oxide for 14, 21 or 35 days consistently produced a significant decrease both in body weight gain and in weight of major organs. The cytochrome p-450 level and aminopyrine N-dimethylase activity in the liver of male rats exposed to 20 percent nitrous oxide for 14 to 21 days were significantly lower than those in controls. The aniline hydroxylase activity was inhibited in 14 day exposure groups.

The drug-metabolizing enzyme activity in the testes appeared to be the most susceptible to nitrous oxide exposure having an effect of general enhancement. There was a three-fold increase in the aminopyrine N-dimethylase activity in the testes of rats exposed to 5 percent nitrous oxide for 30 days. The enhancement of this enzyme activity was consistent in all three nitrous exposure levels (1%, 5% and 20%) and all exposure periods (7, 14, 21, 35, 42 and 84 days).

Pregnant Sprague-Dawley rats exposed to 20% nitrous oxide from day one of gestation to term showed a marked decrease in fetal weight, an increase in resorption rate (57.4%) over the chamber (1.8%) and room controls (4%). The results indicated that these changes were caused by the nitrous oxide in the chamber.

SIGNIFICANCE TO NIOSH:

Studies with laboratory animal exposure are essential in establishing nitrous oxide as the causative agent for toxic effects observed among dentist, their staff, and their families, or whether some other factor peculiar to dentistry is responsible. Such studies can also be useful in providing information for a recommended maximum allowable level of nitrous oxide.

PUBLICATIONS RESULTING FROM THIS GRANT:

- "Effects of low-level nitrous oxide exposures on drug-metabolizing enzymes," presented at the International Association for Dental Research 57th General session, New Orleans, LA., March 31, 1979; J. Dent. Res., 58A, 310, Abstr. No 875.

- "Biochemical Toxicology of Chronic Nitrous Oxide Exposures." Presented at the American Society for Pharmacology and Experimental Therapeutics Fall meeting, Portland, OR., August 22, 1979; Pharmacologist, 21, 216, Abstr. No. 381 (1979).

PERIOD COVERED: December 27, 1979 - December 27, 1980

Reproductive Effects/
Epidemiology/Sampling
Methods/Physical Agents

TITLE: Anesthetic Exposure and Health of Dental Personnel

PROJECT: 5 R01 OH00775-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Ellis N. Cohen, M.D.
Department of Anesthesia
Stanford, CA 94305

GRANTEE INSTITUTION: Stanford University

OBJECTIVES:

- To conduct a comprehensive epidemiologic survey investigating possible health hazards present in the dental operatory involving dentists and their assistants
- To separate the effects of nitrous oxide from other inhalation anesthetics
- To determine the effect of cigarette smoking on fetal viability and the development of fetal abnormalities
- To determine the effect of an inhalation anesthetic during a given trimester on fetal outcome

METHODOLOGY:

This investigation utilized specially prepared questionnaires, which were mailed to a representative segment of the approximately 100,000 members of the American Dental Association and a random sample of their 150,000 dental assistants. Two consecutive mailings were followed by personal telephone calls to non-respondents.

PROGRESS & ACCOMPLISHMENTS:

The results of the study indicated an increased incidence of health problems in those dentists and dental assistants exposed to the anesthetic gasses in the dental operatory, compared to those individuals not exposed. Separate analysis by anesthetic agents indicated that nitrous oxide alone is associated with an increased rate of adverse response.

SIGNIFICANCE TO NIOSH:

The results of this survey will provide a significant contribution to the knowledge regarding health hazards among dental anesthetic exposed personnel.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Occupational Disease in Dentistry and Chronic Exposure to Trace Anesthetic Gasses:1980: Journal of the American Dental Association. v. 101, p. 21-23.

PERIOD COVERED: June 1, 1979 - November 30, 1980

Reproductive Effects/Physical
Agents/Animal/Toxicology/
In Vivo

TITLE: Effects of Pesticides on Reproductive Development

PROJECT: 5 R01 OH00835-02

PRINCIPAL INVESTIGATOR & ADDRESS:
William J. Swartz, Ph.D.
1542 Tulane Avenue
New Orleans, LA 70112

GRANTEE INSTITUTION: Louisiana State University

OBJECTIVES:

- To determine the effects of four commonly used pesticides on specific stages of reproductive development and adult female reproductive function
- To characterize some occupational hazards that confront both pregnant and non-pregnant females engaged in occupations in which pesticide exposure is likely
- To explore the effects of pesticide exposure on embryonic gonadal development and on basic reproductive processes of the sexually mature female

METHODOLOGY:

Both chick and mouse embryos were exposed to a single pesticide during the period of gonadal development. The effects of pesticides on normal embryological development of the gonads, sex, determination, and histochemical alteration in enzyme activity in both primordial germ and cells (PGCs) and other cellular components of the gonads will be investigated.

Female mice exposed prenatally to pesticides will be allowed to reach sexual maturity in order to determine whether embryonic exposure to pesticides can cause deleterious effects on basic ovarian functions which remain undetected until the period of sexual maturity. Measurements of the ability of the ovaries of the offspring to elicit an ovulatory response to exogenous gonadotropins, and of the capacity of the ovarian oocytes to undergo normal meiosis will be used to assess these physiological parameters in ovaries of mice exposed to pesticides when sexually mature. A histochemical study of specific enzymes in the different cellular components of the ovary will also be performed.

PROGRESS & ACCOMPLISHMENTS:

Baseline data were obtained on the onset and distribution of acid and alkaline phosphatases in the early chick embryo.

SIGNIFICANCE TO NIOSH:

The exposure of pesticides on women and their offspring (prior or during pregnancy) have not been given much attention. Previous studies have demonstrated that pesticides can result in a decrease in the number of viable fetuses. No attention has been directed toward any disturbances in the survivors.

The potential hazards that exist for the increasing number of women engaged in types of employment in which exposure to pesticides have not been clearly elucidated. Information obtained from this study will provide reliable means for evaluating the response of the developing and adult female reproduction system to qesticide exposure. Therefore, industrial safety warnings n be issued which explictly indicate the risks so standards can be devised to lower such risks.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Stone, S., M.D. and Swartz, W.M., Ph.D.:1979: A Syndrome Characterized by Recurrent Symptomatic Functional Ovarian Cysts in Young Women. American Journal of Obstetics and Gynecology. v. 134, p. 310-315.
- Schoetz, A., and Swartz, W.: 1979: Intrafollicular Cumlus Cell Transformations Associated with Oocyte Maturation Following Gonadotrophic Hormone Stimulation of Adult Mice. Journal of Experimental Zoology. v. 207.

PERIOD COVERED: April 1, 1979 - March 31, 1980

Reproductive Effects/Cancer/
Human/Physical Agents

TITLE: Occupational Exposures and Rates of DNA Damage

PROJECT: 1 R01 OH00856-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Lawrence J. Fine, M.D.
Rm. 1502, SPHI
Dept. of Environmental
and Industrial Health
Ann Arbor, MI 48109

GRANTEE INSTITUTION: University of Michigan

OBJECTIVES:

- To investigate the relationship between DNA damage and exposure to carcinogens or mutagens in selected occupations
- To compare the rates of sister chromatid exchanges (SCEs) between control and exposed groups of workers from industrial processes which result in exposure to at least one suspected carcinogen or chemical which damages DNA in non-human tests systems
- To compare the rates of SCEs to chromosome aberrations in exposures previously associated with elevated rates of chromosome aberrations (benzene, vinyl chloride, acrylonitrile)
- To compare the rates of SCEs to chromosome aberrations in exposures to potent carcinogens or mutagens (ethylene oxide, coke oven fumes, acrylonitrile)
- To examine the feasibility of using the urinary excretion of mutagenic chemicals as a measure of dose in some occupational environments where other measures of dose exist and exposures to multiple mutagens may occur
- To attempt to estimate total dose of mutagenic exposure by use of Salmonella microsome analysis of air samples in occupational environments where multiple exposure occur
- To attempt to develop dose-response relationships between levels of exposure and levels of DNA damage for all exposures investigated

METHODOLOGY:

The major portion of this study consisted of a series of cross-sectional comparisons of exposed and non-exposed workers, matched on age and sex, with regard to frequencies of chromosome aberrations and SCE. A sample of about 20 subjects in each exposure category was statistically evaluated.

Selection of comparison (non-exposed) groups was made from the same occupational cohorts as the exposed subjects. Potential confounding factors such as age, sex, smoking, and radiation were taken into consideration.

PROGRESS & ACCOMPLISHMENTS:

Initial results suggest that sister chromatid exchanges are an easier test to perform than chromosome aberrations in detecting DNA damage. By using simple methods of chemical analysis with high pressure liquid chromatography, investigators hope to separate mutagenic substances which are the result of cigarette smoking from those which are the results of occupational exposures. Initial studies of workers exposed to Acrylonitrile do not show a higher rate of sister chromatid exchanges.

SIGNFICANCE TO NIOSH:

The camparison of the relative sensitivities of chromosome aberrations and sister chromatid exchanges in detecting genetic injury will be a possible biologic marker of elevated cancer risk.

A better test for the detection of DNA damage caused by environmental exposures would improve the ability to identify new occupational carcinogens and to monitor for the effects of past exposures to known carcinogens.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 1, 1979 - August 31, 1980

Reproductive Effects/Physical Agents/Epidemiological

TITLE: Endocrine Functions of Workers Exposed to PBB and PBBO

PROJECT: 1 R01 OH01034-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Ora Bialik, Ph.D.
420 Service Drive S2
Philadelphia, PA 19104

GRANTEE INSTITUTION: University of Pennsylvania

OBJECTIVES:

- To determine if the agent(s) decabromobyphenyl (PBB), decabromobiphenyl oxide (PBBO), or PBB and PBBO together are associated with adverse effects on thyroid and/or reproductive endocrine function
- To determine whether there is a relationship between estimated grades of exposure to PBB and/or PBBO agents and health effects
- To determine whether there is a time dependent (induction/chronicity) health effect of PBB and/or PBBO agents

METHODOLOGY:

A field study will be conducted of a cohort of workers engaged in the manufacture of PBB and PBBO from 1973 to 1980, focusing on thyroid function tests and on reproductive function tests. Control workers will also be selected. Industrial hygiene methods will be used to provide estimates of grades of exposure.

The tests of endocrine function will be treated as dependent variables. Age, exposure levels, and months since first and last employment will be treated as dependent variables. Stepwise regression procedures and factor analysis will be used to examine the relationships between variables.

PROGRESS & ACCOMPLISHMENTS:

This is a new grant. Progress and accomplishments will be reported in the FY 81 grant report.

SIGNIFICANCE TO NIOSH:

Data from this study should contribute to a better understanding of the general relationship between exposure to halogenated hydrocarbons, PCBs, and human health.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date.

PERIOD COVERED: August 1, 1980 - July 31, 1981

TITLE: Immune Injury in Occupational Respiratory Disease

PROJECT: 2 R01 OH00360-09

PRINCIPAL INVESTIGATOR & ADDRESS:
Robert Burrell, Ph.D.
Dept. of Microbiology
Morgantown, WV 26506

GRANTEE INSTITUTION: West Virginia University

OBJECTIVES:

- To extend observations of the in vivo pulmonary activities of inhaled Aspergillus spores to the thermoactinomycetes involved in hypersensitivity pneumonitis, thermoactinomyces and micropolyspora faeni
- To compare the endotoxin like properties of T. vulgaris and M. faeni with known enterobacterial lipopolysaccharides
- To evaluate the inflammatory changes induced in the lung by inhalation of M. faeni spores, cotton or bract dust, E. coli and purified endotoxin aerosols
- To evaluate the effects of inflammatory changes on respiratory immunization with soluble or particulate antigens
- To study the effects of agents such as steroids and sodium cromoglycate on the inhibition of the changes brought about by aerosol inhalation
- To establish in the local and systemic cell-mediated immunocompetence of lymphoid cells obtained from the lungs and blood of normal unimmunized experimental animals with respect to in vitro assays
- To prepare a protein antigen (human serum albumin) in both a soluble and a particulate form for aerosol immunization
- To develop appropriate immunization protocols which will deliver the antigen in both forms to the lower respiratory tract in equal amounts
- To compare the effect of local respiratory immunization with a soluble and particulate form of protein antigen on the induction of local and systemic cell-mediated immunity
- To determine the effect of acute vs chronic exposure to the antigen in both forms on the local and systemic cellular immune status

METHODOLOGY:

Bacterial cultures were grown on tryptose-glucose-yeast extract agar or broth, washed, and diluted to a standard suspension by nephelometric standardization. Fungi were grown in aerated-shake cultures in glucose-polypeptone broth, washed, homogenized, and passed through a freeze press. These suspensions were used in both in vitro and in vivo tests.

Animals used in this investigation included mice, guinea pigs, and rabbits. All animal aerosol exposures were conducted in self-designed equipment constructed in such a manner that only the animals' heads were exposed. Guinea pigs were anesthetized with barbital, the rabbits with chlorpromazine, and the mice simply restrained by individual holders. A total of eight animals in each species were used for each experiment.

PROGRESS & ACCOMPLISHMENTS:

It was shown that T. vulgaris and M. faeni do not contain endotoxins but their biologic properties were associated with peptidoglycan. This material activates complement and is mitogenic for lymphocytes.

Inhalation of ubiquitous endotoxin containing bacteria, if followed within a certain time by intravenous exposure of a similar organism will result in a lethal hemorrhagic reaction in the lung which can be inhibited by indomethacin, thus pointing to the role of prostaglandins in the response.

SIGNIFICANCE TO NIOSH:

This research focuses on the significance of inhaling dusts generated in the occupational environment. Studies show that pulmonary injury need not be caused solely by well known pathogens such as M. faeni, but rather that ubiquitous microorganisms, such as E. coli, may be important contributers to lung disease under certain conditions.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Burrell, R., and Pokorney, D.:1979: Mediators of Experimental Hypersensitivity Pneumonitis. Int. Archs. Allergy Appl. Immun. 55:161
- Burrell, R. Law, F.W., and Olenchock:1978: The Role of Precipitins in Allergic Lung Disease Life Sciences, vol. 22, p. 1685-1690.
- Demaria, T.F. and Burrell, R.: The Effects of Inhaled Endotoxin-containing Bacteria, Environ. Res. v. 23, In press.

- Smith, S.M., Burrell, R. and Snyder, I.S.:1978: Infection and Immunity, Complement Activation by Cell Wall Fractions of Micropolyspora faeni, vol. 22, No. 2, p. 568-574.
- Smith, S.M., Snyder, I.S., and Burrell, R.:1979: Mitogenic Responses to Micropolyspora faeni Cell Walls. Submitte to: J. Allergy Clin. Immunol.

PERIOD COVERED: September 1, 1979 - August 31, 1980

blank page

Respiratory Diseases/
Physical Agents/In Vivo/
Animal/In Vitro

TITLE: Respiratory Tract Irritants; Mechanisms and Tolerance

PROJECT: 5 R01 OH00367-09

PRINCIPAL INVESTIGATOR & ADDRESS:

Yves C. Alarie, Ph.D.
Department of Industrial
Environmental Health Sciences
Graduate School of
Public Health
130 Desoto Street
Pittsburgh, PA 15261

GRANTEE INSTITUTION: University of Pittsburgh

OBJECTIVES:

- To establish safe levels of exposure for airborne chemicals having irritating properties on the respiratory system
- To establish mechanisms by which cummulative effects of isocyanates may be investigated
- To evaluate the potency of airborne chemicals as pulmonary irritants and make valid comparisons among such irritants
- To delineate the extent of potent irritant interactions with DNA in alveolar macrophages

METHODOLOGY:

This investigation uses the BALB/c strain of mice in three in vivo short term animal bioassays. The mice were anesthetized with pentobarbital and a tracheal cannula was inserted. The mice were then inserted in a plethymograph, and exposed to certain airborne chemicals. Respiratory rates were monitored as a function of time. DNA and chromosomal damage have been and are being investigated by using 5-bromodeoxyuridine.

PROGRESS & ACCOMPLISHMENTS:

Sister chromatid exchange frequencies were observed in bone marrow, liver cells, and alveolar macrophages in mice exposed to styrene. Similar increases were also found following inhalation of aerosols of urethane. The effects of toluene diisocyanate and other diisocyanates will be elucidated.

SIGNIFICANCE TO NIOSH:

The results of this study should provide an important tool to predict safe levels of human exposure to airborne chemical irritants in the work place.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Barrow, C.S., Lucia, H., Stock, M.F. and Alarie, Y.:1979: Development of Methodologies to Assess the Relative Hazards From Thermal Decomposition Products of Polymeric Materials. Am. Ind. Hyg. Assoc. J. 40:408.
- Connor, M.K., Alarie, Y., and Dombroske, R.L.:1979: Sister Chromatic Exchange in Regenerating Liver and Bone Marrow Cells of Mice Exposed to Styrene. Toxicol. Appl. Pharmacol. 50:365.
- Conner, M.K., Alarie, Y., Dombroske, R.L.:1979: Sister Chromatic Exchange in Murine Alveolar Macrophages, Regenerating Liver and Bone Marrow Cells - A Simultaneous Multicellular in vivo Assay. Chromosoma (Berl). 74:51
- Kane, L.E., Barrow, C.S., Alarie, Y.:1979: A Short Term Test to Predict Acceptable Levels of Exposure to Airborne Sensory Irritants. Am. Ind. Hyg. Assoc. J. 40:207.
- Sangha, G.K., and Alarie, Y.:1979: Sensory Irritation by Toluene Diisocyanate in Single and Repeated Exposures. Toxicol. Appl. Pharmacol. 50:533.
- Kane, L.E. and Alarie, Y.:1979: Interaction of Sulfur Dioxide and Acrolein as Sensory Irritants. Toxicol. App. Pharmacol. v. 48:305.
- Kane, L.E. and Alarie, Y.:1980: Evaluation of Sensory Irritation from some Common Industrial Solvents. Am. Ind. Hyg. Assoc. J. v. 41:451.
- Conner, M.K., Alarie, Y. and Dombroske, R.L.: Sister Chromatid Exchange in Murine Alveolar Macrophages, Bone Marrow and Regenerating Liver Cells Induced by Styrene Inhalation. Toxicol. App. Pharmacol. (In press).

PERIOD COVERED: November 1, 1979 - September 30, 1980

Respiratory Diseases/
Epidemiology/Physical
Agents/Animal

TITLE: Pathogenesis of Allergic Pulmonary Aspergillosis

PROJECT: 5 R01 OH00398-06

PRINCIPAL INVESTIGATOR & ADDRESS:

Raymond G. Slavin, M.D.
1402 South Grand Boulevard
St. Louis, MO 63104

GRANTEE INSTITUTION:

St. Louis University School of Medicine

OBJECTIVES:

- To investigate the inflammatory response and alteration of tissue due to aspergillus by studying the interaction of monkey IgG and human IgE in monkey skin
- To investigate the role of cell mediated immunity in the monkey model of allergic aspergillosis
- To establish an animal model of allergic aspergillosis in non-human primates
- To continue studies on the epidemiology of allergic aspergillosis
- To study the atmospheric burden of A. fumigatus in the St. Louis area

METHODOLOGY:

Immunized and unimmunized monkeys with and without IgE precipitating antibody to aspergillus fumigatus (AF) were injected at multiple sites intradermally with normal human serum on human serum rich in IgE against AF. Each site was injected with AF one day later. Serial skin biopsies were taken and light microscopic immunofluorescent and electron microscopic studies were performed.

In vitro studies on lymphocyte transformation in the monkey were also conducted.

Two monkeys were used to establish a primate model of allergic aspergillosis. Monkey A received no immunization and had no precipitating antibody to A. fumigatus. Monkey B was immunized with A. fumigatus and developed strong precipitating antibody in his serum to A. fumigatus.

Spore traps were placed on the roof of a building is St. Louis and atmospheric counts of A. fumigatus were collected.

PROGRESS & ACCOMPLISHMENTS:

The most profound skin changes in the monkeys were associated with similar antibody (IgE) and human antibody (IgE) depected against AF. The skin appeared to mirror inflammatory changes seen in the lung in the primate model of allergic bronchopulmonary aspergillosis.

In vitro studies with aspergillosis extracts continue to be negative. The immunized monkeys demonstrated *in vitro* lymphocyte response of AF.

Upon concentration of lavage fluid, both the experimental monkey and the control monkey demonstrated IgA, IgG, and IgM, but only the experimental monkey had antibody activity directed toward AF. Studies indicated that the A. *fumigatus* spore counts in St. Louis were comparable to those in Great Britain. The exposure to A. *fumigatus* is at least as great in the U.S. as it is in Great Britian.

SIGNIFICANCE TO NIOSH:

The results of this investigation should help determine the tissue response to IgG, IgE, and A. *fumigatus*. In addition, the results should provide a tool to elucidate the immune mechanism responsible for allergic aspergillosis. Finally, the studies will allow the comparison of A. *fumigatus* levels in the United States and Great Britain to explain the different incidence of allergic aspergilliosis in these countries.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Slavin, R.G.:1980: Diagnostic Tests in Clinial Allergy. Postgraduate Medicine, v. 67, No. 3, p. 72.
- Slavin, R.G., Fischer, V.W., Hutcheson, P.S., and T sai, C.C.:1980: Skin Tests in a Primate Model of Allergic Bronchopulmonary Aspergillosis. Journal of International Archives of Allergy. (Accepted for publication.)

PERIOD COVERED: August 1, 1979 - July 31, 1980

Respiratory Diseases/
Toxicology/In Vitro/Human/
Animal

TITLE: Anesthetic Metabolism--Toxic Effects in Operating Room Personnel

PROJECT: 5 R01 OH00622-03

PRINICPAL INVESTIGATOR & ADDRESS: James Trudell, Ph.D.
300 Pasteur Drive
Stanford, CA 94305

GRANTEE INSTITUTION: Stanford University

OBJECTIVES:

- To continue investigation of the metabolism of two commonly used anesthetics, halothane and nitrous oxide
- To establish a possible association between this metabolism and long-term toxicity
- To initiate an in vitro study of the binding of halothane metabolites to protein and phospholipids using reconstituted human liver cytochrome P-450

METHODOLOGY:

This study was conducted using a series of male and female rats that were exposed in groups to $^{15}N_2$. The head space of the chamber was measured for the appearance of metabolized $^{15}N_2$ as either nitrogen gas or ammonia. Urine and feces samples were collected separately. Following measurements of total $^{15}N_2$ content in the urine samples efforts were to separate and identify the individual metabolites.

PROGRESS & ACCOMPLISHMENTS:

Studies of the metabolism inhaled anesthetic halothane, have been conducted. Investigators found three volatile metabolites of halothane in the expired air of human patients under clinical halothane anesthesia. The testing of volatile metabolites for mutagenicity in the Ames Salmonella assay, a modified log growth phase salmonella assay, and a growth inhibition assay have been developed. This test has shown that an unsaturated volatile metabolite is a weak mutagen. A reconstituted cytochrome P-450-phospholipid vesicle system for producing these metabolites in an in vitro system has also been developed.

SIGNIFICANCE TO NIOSH:

Epidemiological studies have indicated an increased miscarriage rate, congenital abnormalities in children, and an increase in liver disease in individuals exposed to the operating room anesthetic-contaminated environment. Definition of the mechanism(s) involved in such toxicity is critical to the health of occupationally-exposed operating room personnel. Additionally, information derived from this research may aid in selection criteria for "safer" or "safest" anesthetics and also may provide the necessary data for development and enforcement of effective programs of waste gas scavenging in operating rooms.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Sharp, J.H., Trudell, J.R., Cohen, E.N.: 1979: Volatile Metabolites and Decomposition Products of Halothane in Man, Anesthesiology, v. 50:2-8.
- Edmunds, H.N., Trudell, J.R., Baden, J.M., Simmon, V.F.:1979: Mutagenicity Studies with Volatile Metabolites of Halothane Anesthesiology, v. 51:424-429.
- Bosterling, B., Dawson, J.H., Hilderbrandt, A.G., Stier, A., and Trudell, J.R.:1979: Reconstitution of Cytochrome P-450 and NADPH-Cytochrome P-450 Reductase into Phospholipid Vesicles: Characterization of Structure and Metabolic Activity, Mol. Pharmacol, v. 16:332-342.
- Edmunds, H.N. and Sachdev, K.: A Simple Implantable Halothane Delivery System. Anesthesiology (In press).
- Cohen, E.W.: Anesthetic Exposure in the Workplace, P.S.G. Publishing Co., Littleton, MA (In press).

PERIOD COVERED: June 1, 1979 - May 31, 1980

Respiratory Diseases/Physical
Agents/In Vitro/Human/Animal

TITLE: Industrial Dust Interaction with Respiratory Mucosa

PROJECT: 5 R01 OH00653-03

PRINCIPAL INVESTIGATOR & ADDRESS:

John E. Craighead, M.D.
Medical Alumni Building
Burlington, VT 05405

GRANTEE INSTITUTION: University of Vermont

OBJECTIVES:

- To document the uptake, transport, localization and elimination of selected industrial and environmental dusts by respiratory mucosa maintained under controlled conditions in organ cultures
- To monitor the acute and chronic effects of environmental dusts on mucosal cell structure, metabolism, replication and differentiation
- To document the effects of selected industrial and environmental dusts on the secretions of mucins of various chemical species by respiratory tract tissues
- To assess the effects of viral infection on the response of the porcine respiratory epithelium to these dusts
- To compare the interaction of porcine and human (smokers and non-smokers) respiratory tract tissue with these dusts

METHODOLOGY:

In this study, the effects of dusts on human tracheobronchial mucosa in organ culture were explored. Suckling porcine tracheobronchial explants will be used as a model system for experimentation. Human tissues from smokers and non-smokers were obtained after thoracotomy and used for comparative studies. After precipitation of known amounts of dusts onto cultures of respiratory epithelium, aspects of cellular metabolism and the composition of mucin secretions were assessed biochemically and correlated with the morphology by light, and electron microscopic observations.

PROGRESS & ACCOMPLISHMENTS:

Studies have been conducted with three types of asbestos, ferric oxide, talc and carbon. Insights have been gained into the mechanisms whereby different types of asbestos interact with the plasma membrane of the cell. The study demonstrated that both chrysotile and crocidolite asbestos enhance the replication of epithelial cells when introduced at the time of cell seeding, whereas mineral fibers have no effect after growth has proceeded for periods of 24 to 48 hours. Initial work has been undertaken on the interaction of aluminum silicates with erythrocytes. The mechanism whereby chrysotile induces release of mucins by the guinea pig tracheal epithelium has been examined.

SIGNIFICANCE TO NIOSH:

This study is designed to elucidate the cellular changes occurring consequent to particulate impingement upon respiratory epithelium and uptake by mucosal cells. Such information may be indicative of epithelial responses in the early stages of carcinogenesis or chronic respiratory disease resulting from occupational dust exposure.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Mossman, B.T., Bradley, B.J. and Craighead, J.E.: 1979: Comparative Cytotoxicity of Chrysotile and Crocidolite Asbestos in Hamster Tracheal Epithelial Cells, Fed. Proc. 38:1352.
- Bradley, B.J., Bellomo, S.C. and Craighead, J.E.: 1979: Interaction of Chrysotile Asbestos with Human Erythrocytes. Fed. Proc. 38:1352.
- Mossman, B.T. and Craighead, J.E.: 1979: Induction of Neoplasms after Implantation of Hamster Trachea Exposed in vitro to 3-methylcholarthrene on Ferris Oxide. Proc. Amer. Assoc. Cancer Res. 20:228.
- Mossman, B.T. and Craighead, J.E.: 1979:In vivo and in vitro Studies with Asbestos. Amer. Rev. Resp. Dis. In press.
- Craighead, J.E., Mossman, B.T., and Bradley, B.J.: 1979: Comparative Biologic Effects of Chrysotile and Crocidolite Asbestos. Env. Health Perspec. In press.
- Mossman, B.T. and Craighead, J.E.: 1979: Use of Hamster Tracheal Organ Cultures for Assessing the Cocarcinogenic Effects of Inorganic Particulates on the Respiratory Epithelium. Prog. Exp. Tumor Res. 24. In press.
- Craighead, J.E. and Mossman, B.T: 1979: Carcinomas of Tracheal Origin Induced in Hamsters by Topical Application of 3-methylcholanthrene. Prog. Exp. Tumor Res. 24. In press.
- Mossman, B.T., Adler, K.B., and Craighead, J.E.: 1979: Interaction of Mineral Dusts with Organ and Cell Cultures Derived from Hamster Tracheal Epithelium Proc. Intern. Workshop on Mineral Dusts. In press.

- Mossman, B.T. and Craighead, J.E.: 1980: Asbestos-Induced Epithelial Changes in Organ Cultures of Hamster Tracheal Inhibition by the Vitamin A Analog, Retinyl Methyl Ether. Science v. 207, p. 311-313.
- Craighead, J.E., Mossman, B.T., Bradley, B.J.:1980: Comparative Studies on the Cytotoxicity of Amphibole and Serpentine Asbestos, Env. Health Perspec., v. 34, p. 37-46.
- Mossman, B.T., and Craighead, J.E.:1979: Use of Hamster Tracheal Organ Cultures for Assessing the Cocarcinogenic Effects of Inorganic Particulates on the Respiratory Epithelium. Prog. Exp. Tumor Res. v. 24, p. 37-47.
- Craighead, J.E., and Mossman, B.T.:1979: Carcinoma Induction by the 3-Methyl-Cholanthrene in Hamster Tracheal Tissue Implanted in Syngeneic Animals. Prog. Exp. Tumor Res. v. 24, p. 48-60.
- Vallyathan, N.V., Brody, A.R., and Craighead, J.E.: 1980: Biological Standard for Energy Dispersive X-ray Analysis. J. Environ. Pathol. Toxicol. v. 3, p. 269-280.
- Vallyathan, N.V., Green, H.Y., Craighead, J.E.: Recent Advances in the Study of Pneumoroniosis, Pathology Annual. In press
- Mossman, B.T., Ezerman, E.B., Abler, K.B., Craighead, J.E.: Isolation and Spontaneious Transformation of Hamster Tracheal Epithelial Cells. Cancer Res. In press
- Mossman. B.T., and Craighead, J.E.: Mechanisms of Asbestos Cocarcinogenesis. Environ. Res. In press

PERIOD COVERED: August 1, 1979 - July 31, 1980

Respiratory Diseases/Physical
Agents/In Vivo/Animal

TITLE: Pulmonary Dust Retention and Occupational Lung Disease

PROJECT: 2 R01 OH00678-03

PRINCIPAL INVESTIGATOR & ADDRESS:

Morton Lippmann, Ph.D.
N.Y.U. Medical Center
550 First Avenue,
New York, NY 10016

GRANTEE INSTITUTION: New York University

OBJECTIVE:

- To quantitatively characterize transfer rates and storage sites for respirable particles of coal, ferric oxide, tantalum and polystyrene latex with defined size, shape and concentration, and for short and long fibers

METHODOLOGY:

Particle retention within thorax and tracheal lymph modes following a single brief aerosol inhalation was measured in rabbits and donkeys, by in vivo detection of radio-nucleides within the particles, and ferromagnetic particles by remnant magnetism. Comparisons were then made with complementary data gathered from the same animals after serial sacrifice.

PROGRESS & ACCOMPLISHMENTS:

The results from this investigation led to the development and testing for exposure of various aerosols. An external gamma detection system for in vivo measurements was modified, tested, and evaluated. The remnant magnetic measurement techniques were also further developed for this study.

SIGNIFICANCE TO NIOSH:

The results should provide an improved basis for characterizing the toxic dose associated with inhalation of airborne contaminants.

PUBLICATIONS RESULTING FORM THIS GRANT:

- Halpern, M., Williamson, S.J., Spektor, D.M., Schlesinger, R.B., Lippmann, M.: Remnant Magnetic Fields for Measuring Particle Retention and Distribution in the Lungs, Experimental Lung Research. In press.
- Robinson, S.E., and Freedman, A.P.: Analytic Methods for Magnetopneumography, Third Workshop on Biomagnetism. In press.

PERIOD COVERED: December 1, 1979 - November 30, 1980

Respiratory Diseases/Cancer/
In Vitro/Animal/Physical Agent

TITLE: Pulmonary Effects of Vinyl Chloride

PROJECT: 5 R01 OH00681-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Yasunosuke Suzuki, M.D.
Environmental Sciences Laboratory
Fifth Avenue and 100th Streets
New York, NY 10029

GRANTEE INSTITUTION: Mt. Sinai School of Medicine

OBJECTIVES:

- To study oncogenic effects of vinyl chloride on mouse lung
- To observe processes of formation of neoplastic cells from precursor via the pre-neoplastic cell in the lung at the ultrastructure level
- To characterize the non-neoplastic pulmonary damage by vinyl chloride in mice and hamsters
- To evaluate vinyl chloride induced lesions in the lungs of vinyl chloride workers

METHODOLOGY:

This investigation uses mice and hamsters as the laboratory animal models. These animals are exposed to various levels and concentrations (2,500 ppm, and 600 ppm, 5 hours a day, 5 days a week) of vinyl chloride. The various exposure times do not exceed six months. After the development of pulmonary tumors, the animals are sacrificed. The tumors will be studied microscopically.

PROGRESS & ACCOMPLISHMENTS:

Light and electron microscopy of lungs of 27 mice that had been exposed to vinyl chloride monomer revealed that pulmonary tumors were induced in 26 of the 27 experimental animals.

SIGNIFICANCE TO NIOSH:

The results from these animal studies may provide useful information for evaluation of the pulmonary effects of vinyl chloride in the more complex human situation, especially in the workplace.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Suzuki, Y.:1979: Types of Known Neoplastic Effects of Vinyl Chloride. Journal of Environmental Research, p. 235-253.
- Suzuki, Y.: Neoplastic and Known Osoplastic Effects of Vinyl Chloride in Mouse Rung. Journal of Environmental Health Prospects. In press.

PERIOD COVERED: December 1 1979 - November 30, 1980

Respiratory Diseases/Clinical
Studies/In Vitro/Human/
Epidemiology

TITLE: Hypersensitivity Lung Disease in Animal Workers

PROJECT: 5 R01 OH00763-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Gerald L. Baum, M.D.
Pulmonary Division
Tel Hashomer, Israel

GRANTEE INSTITUTION: Chaim Sheba Medical Center

OBJECTIVES:

- To determine the extent of asthma and allergic alveolitis apparently caused by animal antigens in groups of individuals occupationally exposed to animals
- To compare the results obtained above with those of a similarly controlled population
- To compare the results of in vitro assay of hypersensitivity with the results of clinical studies in identifying the sensitized individuals
- To study the relationship between the development of asthma or allergic alveolitis and occupational exposure to animals as found in high risk contacts such as veterinarians, animal caretakers, or research technicians

METHODOLOGY:

There are approximately 300 veterinarians in Israel, most of whom work for a prepaid animal health insurance plan. This provides a high degree of accessibility to this test population. Based on preliminary discussions with this group of veterinarians, it is estimated that over 90% of those individuals will participate in the study.

The laboratory animal contacts group will include animal caretakers, laboratory animal handlers, and animal research technicians. These subjects will be drawn from volunteers at the four medical schools in Israel (Jerusalem, Tel Aviv, Haifa, Beersheva) and other research centers with animal facilities. The study will include about 100 of these individuals.

The control subjects will consist of 100 physicians and other paramedical personnel matched for age, sex, and ethnic background with the study groups. The control group will include individuals who have no occupational exposure to animals.

For clinical evaluations, a case study will be obtained by administering questionnaires. These questionnaires are designed to collect information on the subjects' relevant medical history with special emphasis on respiratory disease, possible atopic background, and occupational and environmental history with particular emphasis on contact with animals (species, duration, intensity). The presence of symptoms suggestive of allergic alveolitis (chills, fever, dysperea, cough 4-6 hours after exposure) will be ascertained. A general physical examination will be carried out on each subject with particular attention to the respiratory tract. In addition, blood and skin tests will be included.

PROGRESS & ACCOMPLISHMENTS:

While experiments with animal house workers have not been analyzed in detail, early results indicate that the amount of hypersensitivity seen in this group is less than that encountered in the veterinarians.

SIGNIFICANCE TO NIOSH:

Determination of the relative importance of hypersensitivity to animal urine, serum and/or skin antigens in individuals whose daily occupational activity puts them into sustained contact with animals has significant value.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: July 1, 1979 - June 30, 1980

TITLE: Aflatoxin Exposures of Agricultural Workers II

PROJECT: 1 R01 OH00796-01

PRINCIPAL INVESTIGATOR & ADDRESS:

William R. Burg, Ph.D.
3223 Eden Avenue
Cincinnati, OH 45267

GRANTEE INSTITUTION: University of Cincinnati

OBJECTIVES:

- To determine aflatoxin exposure levels experienced by farmers, truckers, and grain handlers in harvesting corn infested with Aspergillus flavus
- To assess the general air pollution potential
- To determine the extent of the drift of airborne aflatoxin from the fields
- To determine a correlation between airborne levels of aflatoxins and field and local air conditions
- To determine aflatoxin levels in and around several large commercial elevators
- To determine the need for controls to prevent worker exposures
- To determine the levels of aflatoxin in different particulate size fractions
- To determine the need for future epidemiological, medical and animal exposure studies

METHODOLOGY:

Regions of the country with weather and insect conditions expected to promote fungi growth were identified. Samples were then collected from corn fields, and ten specific fields were selected for a detailed sampling.

The samples will be analyzed by the use of a thin layer chromatographic procedure employing a fluorescence detection system. After the experimental work is completed, the data will be analyzed for statistical significance and epidemiological considerations.

PROGRESS & ACCOMPLISHMENTS:

The study has demonstrated that airborne dust generated when handling dry contaminated corn contains aflatoxins and may pose an inhalation hazard.

Samples collected from several farms and a grain elevator have been analyzed. Several analytical methods have been developed for the detection or measurement of aflatoxins in corn. The samples obtained contained large numbers of fungi, including some species known to be potential hazards to humans and animals. Samples from three different farms, six different fields, have been collected. In addition, forty samples from grain elevators were collected. These samples are being analyzed by USDA.

SIGNIFICANCE TO NIOSH:

This study will establish analytical techniques for measuring aflatoxin levels of airborne dust. It will also establish a relationship between bulk corn aflatoxin levels and inhalation levels of workers. It is anticipated that the results of this study may be used to recommend temporary control measures. In addition, the project will provide groundwork for future studies of major contributing factors to cancer in agricultural workers.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Burg, William R., Shotwell, Odette L., Svetlik, Jozef.:1980: Measurements of Airborne Aflatoxins During the Handling of Contaminated Corn. Presented at AIHC. May, 1980.
- Shotwell, O.L., Burg, W.R., and Diller, T.: 1980: Aflatoxin: Analysis of Contaminated Corn Dust. Presented at AIHC, May, 1980.

PERIOD COVERED: March 1, 1979 - February 28, 1980

Respiratory/Epidemiology/
Clinical Studies/Physical
Agents/In Vivo/Animal

TITLE: Respiratory Hazards of Swine Confinement Workers

PROJECT: 5 R01 OH00825-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Kelley J. Donham, D.V.M.
Institute of Agricultural &
Medicine Environmental Health
College of Medicine
Oakdale, IA 52319

GRANTEE INSTITUTION: University of Iowa

OBJECTIVES:

- To conduct a study of the diseases affecting workers in swine confinement strutures
- To study the effects of particulates and gases from swine confinement structures in hamsters and guinea pigs
- To analyze and evaluate toxic gases involved in swine confinement structures

METHODOLOGY:

This investigation consists of epidemiologic, clinical and environmental studies designed to document and characterize the extent that disease occurs in swine confinement workers with emphasis on respiratory disease.

The epidemiologic studies will use data collected by mail and personal interviews to quantify the exposed population, characterize symptoms, and establish a data base to develop cohorts for the clinical studies.

Clinical studies involving four separate cohorts, including a cross-sectional, two environmental challenge studies, and a study of severly affected individuals will be performed to identify the etiology of and predict symptoms and effects of chronic exposure. Animal studies will be carried out to predict pathological effects on the human respiratory tract. The environmental studies will include characterization of particulates in the work environment, quantitation of trace toxic gases, and measurement of gases evolved from the manure pit under different environmental variables.

PROGRESS & ACCOMPLISHMENTS:

A total of 477 questionnaires were received and tabulated. It was found that nearly 70% of the people reported adverse systems associated with work in the swine confinement buildings. The most common coughing reported symptoms were associated with the respiratory tract, i.e., cough, chest tightness, wheezing, excess sputum production, and shortness of breath.

Data from this investigation indicate that in general, the more concentrated the manure, the more hostile the chemical and biological environment within the pit. For example, the total solids are very high (11.4%); the chemical oxygen demand is very high (143,000 mg/l); and the ammonia nitrogen is high (10,200 mg/l). This level of ammonia is far beyond the toxic level of 3,000 mg/l for methane fermentation. It was found that the inhibition of methane fermentation begins at an ammonia nitrogen level of about 1,500 mg/l. These conditions enhanced the production of more toxic gases such as ammonia and hydrogen sulfide.

SIGNIFICANCE TO NIOSH:

The results of this study should provide data that will help characterize the chronic effects of exposure to the swine confinement atmosphere.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1979 - May 31, 1980

Respiratory/Physical Agents/
Analytical Methods
Development/Human

TITLE: Aerosol Deposition in the Human Respiratory System

PROJECT: 1 R01 OH00923-01

PRINCIPAL INVESTIGATOR & ADDRESS:

C.P. Yu, Ph.D.
Dept. of Engineering Science
SUNY at Buffalo
Buffalo, NY 14214

GRANTEE INSTITUTION: Research Foundation of SUNY

OBJECTIVES:

- To predict the total and regional depositions, clearance and retention of airborne particulates in the human respiratory system
- To develop a stochastic model to predict intersubject variability due to variations in lung geometry, breathing pattern, and physiological conditions

METHODOLOGY:

This project involves mathematical modeling and theoretical predictions. Empirical modeling of head deposition was performed to determine the aerosol concentration reaching the trachea. Intersubject variability due to differences in respiratory rate, depth, and pause was studied using a parametric analysis of the deterministic model. In addition, a statistical deposition model was developed to fit the inter-subject variability caused by anatomical differences. A deterministic deposition model will be developed using Horsfield and Cummings' data. Computer programs will be developed for different airway dimensions and number of alveoli.

PROGRESS & ACCOMPLISHMENTS:

A study on inter subject variability of aerosol deposition in the human lung has been made. Results indicate that both airway dimensions and breathing patterns affect deposition.

Calculations on total and regional depositions were made for three different ventilatory states. The results differ from a previous model, particularly for diffusional particles.

The statistical model of head deposition has been completed and will be incorporated with the lung deposition model for further studies. Efforts have been made, with some success, to construct a lung deposition model with asymetrical airways.

SIGNIFICANCE TO NIOSH:

This research is directed toward developing predictive mathematical models of aerosol deposition in the human respiratory system for occupational application. Understanding particle deposition contributes to the elimination of industrial respiratory health hazards and, relates the concentration of airborne particulates to lung disease.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Yu, C.P.:1980: "Intersubject Variability of Aerosol Deposition in Human Lungs," Second International Conference on Mechanics in Medicine and Biology, Osaka, Japan.
- Yu, C.P.:1980: "Mathematical Modeling of Aerosol Deposition in the Human Lung," 13th Aerosol Technology Meeting, Harvard School of Public Health, Boston, Mass.
- Diu, C.K. and Yu, C.P.:1980: "Deposition from Charged Aerosol Flows Through a Two-Dimensional Bend," Journal of Aerosol Science, v. 11, p.391-395.
- Diu, C.K. and Yu, C.P.:1980: "Deposition from Charged Aerosol Flows Through a Pipe Bend," Journal of Aerosol Science, v. 11, p. 397-402.
- Chan, T.L. and Yu, C.P.:1980: "Charge Effects on Particle Deposition in the Human Tracheobronchial Tree," Fifth International Symposium on Inhaled Particles, Wales, England.

PERIOD COVERED: December 1, 1979 - November 30, 1980

blank page

TITLE: Prevention of Accident Head Injury

PROJECT: 5 R01 OH00404-05

PRINCIPAL INVESTIGATOR & ADDRESS:

Alan M. Nahum, M.D.
Department of Surgery
225 Dickinson Street
San Diego, CA 92103

GRANTEE INSTITUTION:

University of California
The Regents of the University
of California at San Diego

OBJECTIVES:

- To study the biomechanics and pathophysiology of closed head injury in the human cadaver
- To develop the human specimen as a model in order to establish relationships between impact parameters, pathophysiological change and indices of head injury
- To continue the study of head impact for new exposures to the side of the head
- To develop a reproducible, experimental, and mathematical model relating head injury with the various force parameters

METHODOLOGY:

A nine accelerometer array and hardware was purchased and a computer data program completed and validated by an independent 10th accelerometer system. This provided the ability to measure and analyze head impact and motion through all phases of the experiment. A series of five full scale experiments were conducted on individual unembalmed pressurized specimens using a side-of-head impact mode. A series of progressively severe impacts were conducted on a single embalmed specimen.

PROGRESS & ACCOMPLISHMENTS:

Correlation of head impact and injury has been accomplished. Differing helmet constructions were evaluated in terms of inpact modfication. A computer head model is now in operation.

SIGNIFICANCE TO NIOSH:

Head injury remains one of the major causes of accidental death. Results from this investigation may provide exposure information for the full range of head impacts which has the potential for establishing the dangerous force level, the present and potential role of head protection devices and possible new head injury severity indices.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Nahum, A.M., Smith, R. and Raasch, F. 1979. Intracranial Pressure Relationships in the Protected and Unprotected Head Proc. 23rd Stapp Car Crash Conference.

PERIOD COVERED: August 1, 1979 - July 31, 1980

Safety/Human/
Administrative Methods/
Testing

TITLE: A Behavioral Approach: Motivational/Financial Impact

PROJECT: 1 R01 OH00777-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Judi Komaki, Ph.D.
Engineering Experiment
Station,
Atlanta, GA 30332

GRANTEE INSTITUTION:

Georgia Institute of
Technology

OBJECTIVES:

- To develop and test the efficacy of a selected psychological technique and the applied behavior analysis approach to facilitate desired safety practices in the work place

METHODOLOGY:

This study was conducted in a poultry processing plant employing 273 individuals in 11 departments. Six departments provided subjects for the study. Behavioral observations and observational codes were established after review of accident reports over five years, with particular focus on the type, circumstances, and possible courses of previous accidents or health related hazards. Interviews and observations were conducted with supervisors and staff focusing on behavior. The Mirvis Behavioral Casting Guide was used to provide an index of the cost effectiveness of improved safety practices and to obtain data.

PROGRESS & ACCOMPLISHMENTS:

The results demonstrate that employees were reminded frequently about safety regulations, and supervisors discussed safety weekly with employees. Feedback was found to be effective over an extended period of time. In addition, the financial assessment of the cost effectiveness of improved safety practices showed considerable savings in both direct and indirect costs. The behaviorial analysis report included the training of personnel as well as their motivation on the job.

SIGNIFICANCE TO NIOSH:

This project will provide NIOSH with significant information relating to cost effective methods of improving safety practices in the workplace. In addition, this project may also provide NIOSH with new information on effective behavior modification methods for improving safety practices in the workplace.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Komaki, J.: Promoting Job Safety and Accident Prevention, In T.J. Coates (ED.), Behavioral Medicine: A Practical Handbook. Champaign, Ill. Research Press, In press.
- Komaki, J., Heinzmann, A. and Lawson, L.: Component Analysis of a Behavioral Safety Program; Effects of Information and Feedback, J. of Applied Psych, In Press.

PERIOD COVERED: January 1, 1979 - June 30, 1980

TITLE: Safety in Grain Bins

PROJECT: 5 R01 OH00849-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Ira J. Ross, Ph.D.
Room 130
Agricultural Engineering
Department
Lexington, KY 40546

GRANTEE INSTITUTION: University of Kentucky

OBJECTIVES:

- To determine the magnitude and character of forces acting on a person trapped in a mass of grain flowing to a bin outlet from bulk storage under normal and faulty grain conditions
- To develop equipment and procedural criteria for preventive safety and emergency techniques to avoid and/or minimize risk for a person entering a grain bin and carry out search, sustain life and complete rescue

METHODOLOGY:

A grain storage test bin approximately 14 feet in diameter and at least 42 feet tall will be constructed at the University of Kentucky grain storage and feed preparation facility. Construction will be near the University of Kentucky facilities so that grain available on the site can be utilized for test purposes and can be stored and handled with existing equipment.

The bin will be used to determine how the rate of grain flow affects the immersion time and the forces acting upon a person trapped in the flow column. These experiments will be conducted under conditions where enveloping flow is fully developed (grain depth less than 20 feet) and where plug flow with impending enveloping flow exists (grain depth greater than 42 feet). Mannequins similar to those used in auto crash studies will be suspended from a load cell centered over the outlet of the test bin. The forces required to hold the mannequin motionless at various depths of partial immersion in the grain flow envelop and complete immersion in the grain flow column up to 20 feet in depth will be determined. These experiments will be replicated at least three times and conducted for at least five different rates of material withdrawal from the bin in the range of 500 to 5000 cubic feet/hour. The rate of descent of the mannequin in the flow envelope and in the flow channel will be determined as a function of the same rates of withdrawal from the bin. These experiments will be conducted with shelled corn and at least one other grain, probably wheat or grain sorghum.

The information gained from these particular experiments will be used in part to evaluate the effectiveness of plain ropes, ropes with harnesses, harnesses with quick catch devices attached to ropes, and bean ladders in preventing entrance into the grain flow column. It is anticipated that their effectiveness will decrease as grain withdrawal rates are increased. The information will be used to determine under what conditions it will be possible to withdraw a person submerged in a flow channel.

PROGRESS & ACCOMPLISHMENTS:

The project is nearing completion and it is anticipated that the full scale bin test will be initiated shortly.

Model bin tests are being conducted to evaluate several of the following variables: the flow of grains, rate of submersion of a simulated body, and the forces imposed on the simulated body.

SIGNIFICANCE TO NIOSH:

This project will provide a data base information on the nature and causes of accidents that occur in commercial and farm grain storage structures which can be used to develop safety equipment, operating procedures, and standards for preventing these accidents. The ultimate contribution of the project should be a reduction in the number of deaths occurring in grain bins each year.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: April 1, 1979 - March 31, 1980

TITLE: Grinding Wheel Crack Detection

PROJECT: 1 R01 OH00969-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Milton C. Shaw, Sc.D.
ECG 247
Tempe, Arizona 85281

GRANTEE INSTITUTION: Arizona State University

OBJECTIVE:

- To develop and evaluate a technique for the detection of cracks in the critical region of a grinding wheel

METHODOLOGY:

Three point modulus of tests will be performed on sulfur graphite material currently used in the lining of bores of grinding wheels, in order to devise a nonconducting liner with nearly the same properties. Three or four wheels with the new sulfur mixture will be spin tested in a wheel manufacturer's plant.

If these are successful, 100 grinding wheels will be ordered and provided with the new liner material. A helical scratch will be filled with electrically conducting paint. A simple method will be designed for determining when the first crack appears as indicated by loss of electrical conductivity in the helical conductor in the bore of the grinding wheel. The mechanics of crack propagation, particularly critical crack size, will be studied in static bending tests on beams cut from previously broken wheels using a diamond cut-off machine. The results of this investigation will be widely disseminated through publications and a special workshop for grinding wheel manufacturers.

PROGRESS & ACCOMPLISHMENTS:

This is a new grant. Progress and accomplishments will be reported in the FY 81 grant report.

SIGNIFICANCE TO NIOSH:

This investigation is expected to develop a method for detecting cracks in grinding wheels that would enable the wheel to be stopped before breaking apart. Thus, the number of serious accidents associated with the use of grinding wheels that occur in workshops may be reduced.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date.

PERIOD COVERED: September 1, 1980 - August 31, 1981

blank page

Other/In Vitro/Toxicology/
Animal

TITLE: Metabolism of Industrial Toxicants

PROJECT: 5 R01 OH00316-15

PRINCIPAL INVESTIGATOR & ADDRESS:

Kenneth C. Leibman, Ph.D.
Health Center
Box J-267
Gainesville, FL 32610

GRANTEE INSTITUTION: University of Florida

OBJECTIVE:

- To study the metabolism of a number of classes of organic industrial chemicals on the NIOSH priority list, including the group of allyl and acrylyl compounds which present toxicological problems in the workplace and the general environment

METHODOLOGY:

The organic substances were studied in vitro through preparation of microsomes and other subcellular portions of liver and other organs of mice, rats, and rabbits. The metabolites were separated and quantified by gas-liquid, liquid-liquid, thin layer, and paper chromatographic techniques.

PROGRESS & ACCOMPLISHMENTS:

The work on the metabolism of allyl alcohol and acrolein was completed and published. A project in the characteristics of cyanide removal from acrylonitrile was also completed and is being summarized for publication. Work in the metabolic activation of acrylamide to an intermediate that selectively destroys certain activities of cytochrome P-450 was presented at the Second Intermediate Symposium on or of Reactive Metabolic Intermediates in Guildford, England. Work on destruction of cytochrome P-450 and of NADPH-cytochrome c reductase was reported at the Federation meetings in Anaheim, California. Progress has been made on the study of acrylamide metabolism.

SIGNIFICANCE TO NIOSH:

This work will provide information on the pathways and mechanisms of biotransformation of several types of industrial and environmental chemicals that constitute known or potential toxicology problems.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Patel, J.M., and Leibmen, K.C.:1978: Microsomal Metabolism of Cyclohexane: Hydroxylation in the Allylic Position. Drug Metab. Dispos. 6:375.

- Town, C., and Leibman, K.C.:1979: In Vitro Dechlorination of Polychlorinated Ethanes by Rat Homogenates. Fed. Proc. 38, 538.
- Patel, J.M. and Leibman, K.C.:1979: Biochemical Effects of Acrolein on Rat Liver and Lungs as Influenced by Various Pretreatments. Fed. Proc. 38, 542.
- Patel, J.M. and Leibman, K.C.: The Biotransformation of Allyl Alcohol and Acrolein in Rat Liver and Lung Preparation. Drug Metab. Dispos. (In press).
- Leibman, K.C., Patel, J.M., and Ortiz, E.: Stability of Lung and Liver Xenobiotic Metubolizing Activities Hyophodezed Micromal Preparations, Fed. Proc. (In press).
- Patel, J.M., Ortiz, E., and Leibman, K.C.: Selective Inactivation of Rat Liver NADPH-Cytochrome and Reductase by Acrolein, Fed. Proc. (In press).

PERIOD COVERED: January 1, 1980 - December 31, 1981

TITLE: Atomic Spectrometry of Occupational Health Samples

PROJECT: 5 R01 OH00739-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Joseph A. Caruso, Ph.D.
Department of Chemistry
Cincinnati, OH 45221

GRANTEE INSTITUTION: University of Cincinnati

OBJECTIVE:

- To develop multi-element analysis schemes at the trace level for occupational health samples by computer controlled rapid scanning and slew spectrometry

METHODOLOGY:

This study is comparing the results of other, proven methods of analysis with the results of the faster, atomic spectrometry method, for trace element analysis to insure accuracy and precision. In addition, computer software is being designed to increase the spectrometer's rate of speed for quick analysis.

PROGRESS & ACCOMPLISHMENTS:

Results from spectrometry on a sample of polybrominated and polychlorinated hydrocarbons biphenyls were excellent in comparison to the usual gas chromatography method utilizing the electron capture detector which is the accepted and less specific method. A manual multielement method was found to determine arsenic, germanium, selenium, and antimony.

A computer control plasma emission spectrometer was developed which will allow analysis of up to 60 elements at less than one minute per element. Thus, a typical ten element analysis requires only five to ten minutes to accomplish. Such analyses are at the part per billion level with precisions of better than three percent. Comparisons with other techniques for the same samples were very favorable.

SIGNIFICANCE TO NIOSH:

A method for evaluating trace element profiles for body tissues and fluids would allow for very early detection of physiological abnormalities or changes, and may therefore, eliminate subsequent health problems.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Mulligan, K.J., Hahn, M.H., Caruso, J.A., and Fricke, F.L.:1979: Camparison of Several Microwave Cavities for the Simultaneous Determination of As, Ge, Se, and Sn by Plasma Emission Spectrometry. *Anal. Chem.*, *51*, 1935.

PERIOD COVERED: January 1, 1979 - December 31, 1980

TITLE: Increase of Toxicity of Trace Anesthetics by UV Light

PROJECT: 5 R01 OH00781-03

PRINCIPAL INVESTIGATOR & ADDRESS:

Joannes H. Karis, M.D.
Box 3094
Durham, NC 27710

GRANTEE INSTITUTION: Duke University

OBJECTIVES:

- To determine if ultraviolet (UV) irradiation by germicidal lamps enhances the toxicity of halothane and other halogenated anesthetics
- To identify the chemical compounds to which halothane is converted by germicidal lamp irradiation.
- To measure the toxicity of these compounds by mortality in mice and rats

METHODOLOGY:

Trace levels of anesthetics released during operations are potential health hazards for operating room personnel. The common anesthetic agents, halothane, enflurane and nitrous oxide can be metabolized in vivo or converted to more reactive compounds in vitro. Ultraviolet light irradiation is used in some operating rooms to decrease intra-operative inflections. Ultraviolet light irradiation may decompose these agents to toxicants either directly or indirectly through ozone or other photochemical reactions. The potential role of photochemical reactions in the inhalation of trace concentrations of these agents by operating room personnel, rats and mice that will be exposed to known concentrations of halothane, enflurane or nitrous oxide with and without light irradiation will be investigated. The wave length of the light source will be varied to determine the nature of the photochemical reaction using fluorescent, germicidal and ultraviolet lamps.

The concentration of the anesthetic agent before and after irradiation will be measured by electron capture gas-liquid chromatography and mass spectrometry. The nature of the decomposition products will be determined and the inhalation toxicity of the irradiated gases will be determined. Conversion of nitrous oxide to nitrogen dioxide and other oxides of nitrogen will be determined chemically. Finally, the concentration of the anesthetic agents and their potential toxic decomposition products will be measured in the operating room. These data will be used to assess the potential human hazards from long term occupational exposure.

PROGRESS & ACCOMPLISHMENTS:

Two approaches were used in the asssessment of the role of lipid peroxidation in halothane hepatotoxicity. Data from these two studies suggest that lipid peroxidation is enhanced during halothane hepatatoxicity. The identification of UV irradiated halothane decomposition products and the determination of acute and subacute toxicity of the halothane decomposition products were completed. Preliminary work showed that ultraviolet irradiation of halothane vapors by germicidal lamps increased the toxicity to mice.

SIGNIFICANCE TO NIOSH:

This research focuses on the identification of decomposition products of airborne contaminants which could be a major hazard to workers and patients exposed to anesthetic gases. In addition, the examination of the role of ultraviolet light in the decomposition process is significant due to its increasing use in operating rooms.

PUBLICATIONS RESULTING FROM THIS GRANT:

- O'Neal, F.O., Karis, J.H. and Menzel, D.B.: 1980: The Effects of Vitamin E on Halothane Hepatotoxicity in Mice, Abstract # 127, Papers of 19th Annual Meeting, Society of Toxicology.

- O'Neal, F.O., Menzel, D.B., Karis, J.H.:1979: Pentane Expiration: A Measure of Halothane Induced Peroxidation, Anesthesiology, 51:5255.

- Karis, J.H., O'Neal, F.O., Menzel, D.B.:1980: Toxicity of Ultraviolet-Irratiated Halothane in Mice, Anesthesiology. (Submitted).

PERIOD COVERED: September 1, 1979 - August 31, 1980

TITLE: Dosimetry for Non-Ionizing Radiation

PROJECT: 1 R01 OH00859-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Glenn E. Fanslow, Ph.D.
122 Coover Hall
College of Engineering
Ames, IA 50011

GRANTEE INSTITUTION: Iowa State University

OBJECTIVES:

- To investigate the development of a passive dosimeter for microwave radiation
- To use the temperature-dependent property of thermoluminescence fade as a means of determining average and accumulated non-ionizing radiation

METHODOLOGY:

This investigation involved the comparison of the thermoluminescence signals of two sensors. Both sensors had temperature variations due to changes in ambient temperature. The temperature of one of the sensors was raised above ambient by an amount related to the non-ionizing radiation present. This higher temperature, was expected to cause more fade in one sensor than the other, and the difference in the thermoluminescence signals from the two sensors would be a measure of the non-ionizing radiation.

PROGRESS & ACCOMPLISHMENTS:

Thermoluminescence dosimetry (TLD) thermo fade characteristics have been determined for $CaSO_4$-manganese, CaF_2 dysproprium and $CaSO_4$ dysproprium. Only CaSO4-manganese has potential for use in this investigation. Radiation tests have been made, but not yet evaluated. Data are still being analyzed.

SIGNIFICANCE TO NIOSH:

The possibility of hazardous radiation from many commercial and industrial sources increases the need for a radiation dosimeter. The low cost involved would help to increase the availability of dosimeters, which would aid in the reduction of the possibile hazardous radiation.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 28, 1979 - August 31, 1980

Other/Physical Agents/
Animal

TITLE: Antigens For Detecting Industrial Hypersensitivity

PROJECT: 1 R01 OOH00865-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Meryl H. Karol, Ph.D.
603 Parran Hall
Pittsburgh, PA 15261

GRANTEE INSTITUTION: University of Pittsburgh

OBJECTIVES:

- To refine the toluene diisocyanate (TDI) Antibody Radioimmunoassay by developing alternative test antigens such as O-Tolyl (Mono) Isocyanate, M-Tolyl (mono) Isocyanate, and Dimethyl Phenyl Isocyanate Protein Conjugates
- To develop test antigens for hypersensitivity to several industrial diisocyanates using monoisocyanate analogues of corresponding industrial diisocyanates
- To determine the immunogenic potencies of low molecular weight industrial chemicals, other than diisocyanates, by using appropriate hapten-protein conjugates and the guinea pig model of industrial asthma

METHODOLOGY:

Sera from TDI - sensitized workers will be obtained for antibody evaluations. Outdated sera will be used as control sera to indicate levels of antibodies in the general population. Sera will be tested for isocyanate antibodies.

Various antigens will be compared for their relative sensitivity in detecting antibodies in sera from persons with TDI hypersensitivity.

Radioassays for IgE antibodies to other diisocyanates of industrial importance hexamethylene diisocyanate (HDI), methane diphenyl diisocyanate (MDI), isophorone diisocyanate (IPDI), NDI and hydrogenated (MDI) will also be developed.

The study will use the guinea pig animal model to evaluate the sensitzing potencies of several industrail chemicals when inhaled as hapten-protein conjugates. Formaldelhyde, acrolein, and ethylenediamine will be included among these chemicals. The synthetic haptenic antigens found to be most effective in detecting antibodies in sensitized guinea pigs will be used to evaluate sera from sensitized workers for similar antibodies.

PROGRESS & ACCOMPLISHMENTS:

Progress and accomplishments will be provided during 1981.

SIGNIFICANCE TO NIOSH:

This study will provide industry with a screening procedures to follow development of disease at the work site. Techniques used appear to be applicable to a variety of allergic reactions probably induced by small - molecular compounds widely used in industry and thus could open up a new field of investigation.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: May 1, 1980 - December 31, 1981

Other/Analytical Methods
Development/Physical
Agents

TITLE: NOVEL LC Multielement Methods for Occupational Health

PROJECT: 5 R01 OH00876-02

PRINCIPAL INVESTIGATOR & ADDRESS:

Peter W. Carr, Ph.D.
Department of Chemistry
Minneapolis, MN 55455

GRANTEE INSTITUTION: University of Minnesota

OBJECTIVE:

- To develop high pressure liguid chromatography (HPLC) methods for the measurement of trace metals, primarily through pre-column derrivitization of the metals with organic ligands to impart a readily detectable property such as intense ultra violet absorption or fluorescense

METHODOLOGY:

This project involves the development of a rapid multi-metal analytical method, based on the formation and separation of fluorescent 8-hydroxy-gunioline metal chelates on either reversed-phase or normal-phase HPLC columns. The metals will be monitored by using combined fluorescence and electrochemical detectors. The work focuses on finding proper chemical conditions for adequate separations and optimization of the fluorescent detection.

PROGRESS & ACCOMPLISHMENTS:

Two distinct types of ligands were tested for potential use in HPLC. It was verified that many metals can be detected with a fluorescence HPLC detector.

The first complete description of the influence that a nonlinear detector has on one's ability to do quantitative analysis by chromatographic methods was developed. When the chromatographic processes were attempted using the Perkin-Elmer 3B LC System, the following results were obtained:

- Regardless of the solvent used, Ni-pyridylazonaphthol (PAN) complex gave sharp peaks, but the peaks coincided with that of PAN and were unretained;

- The chromatography of the other metal complexes in most solvents gave peaks showing considerable tailing and very little retention;

- The presence of a butylamine in any solvent sharpened the peaks and shortened the retention time

Also, findings indicated that the AcAc complexes of beryllium, chromium, cobalt, and manganese can be easily separated by reverse phase HPLC in both water/methanol and water/acetonitrite mixtures. Reverse phase HPLC of metal complexes was demonstrated.

SIGNIFICANCE TO NIOSH:

A combination of modern HPLC and fluorometric detection of metals will provide a rapid and sensitive approach to multielement detection of metals in industrial air contaminant samples.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Carr, P.W.:1980: "Fundamental Predictive Approach to Dipole-Dipole Interactions Based on the Dipole Moment of the Solute and the Dielectric Constant of the Solvent." J. Chromatograph. 194:105.
- Carr, P.W. "A General Treatment of the Effect of Nonlinear Detectors on the Height, Area and Higher Moments of Garisson Chromatographic Peaks." Anal. Chem. (Accepted for Publication).

PERIOD COVERED: September 28, 1979 - August 31, 1980

Other/In Vitro/Toxicology/
Human

TITLE: Mercury Burden and Health Impairment in Dental Auxiliaries

PROJECT: 1 R01 OH00886-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Irving Shapiro, Ph.D.
School of Dental Medicine
4001 Spruce Street,
Philadelphia, PA 19104

GRANTEE INSTITUTION: University of Pennsylvania

OBJECTIVES:

- To examine the relationship between cumulative mercury exposure and chronic health impairment
- To measure in situ the cumulative mercury concentration in the brain and bones of dental chairside auxiliaries who utilized mercury amalgams in dental practice using an x-ray fluorescence technique
- To compare these mercury levels with mercury burdens of a cohort group whose work environment does not include amalgams

METHODOLOGY:

The sample population for this study consists of 300 dental auxiliaries who have had contact with mercury and a cohort of 50 dental auxiliaries who do not use mercury in their practice. Cumulative mercury levels were ascertained by measuring bone and head mercury levels in situ by an x-ray fluoresecence technique that was developed in the investigator's laboratories. The top ten percent of the ranked population are being examined for neurological and renal deficits. Electrodiagnostic studies will measure nerve conduction velocity, denervation, neuromuscular transmission and sensory action potentials. Renal examination includes kidney urinary concentrating function, osmolality and urinary microprotein. The kidney mercury level will also be determined by x-ray fluorescence in the group demonstrating elevated bone mercury. Neuropsychological evaluation is being performed on the ranked upper and lower twenty-five percent of the population. Current mercury exposure levels of these populations is being determined through analysis of blood, urine and hair and correlated with total body mercury burden as determined by x-ray fluorescence.

PROGRESS & ACCOMPLISHMENTS:

The first part of the year was devoted to evaluating the x-ray fluorescence technique. Correlations between x-ray fluorescence sensitivity, tissue density and the effects of overlying tissue were measured. Comparisons were made between the x-ray fluorescence technique and chemical assays of human tissues in vitro were performed. These studies were considered necessary in order to maximize the usefulness of x-ray fluorescense and to be cognizant of its limitations.

In the remaining part of the year the mercury levels in dental auxiliaries were measured. A small percentage of auxiliaries had elevated mercury concentrations in their wrists. This finding may be related to poor mercury hygiene in this group of individuals. Finally, neuropsychological studies have commenced on subjects with high tissue mercury levels and on those with no measurable mercury levels.

SIGNIFICANCE TO NIOSH:

The results of this investigation should provide qualitatively different data from those previously obtained and therefore should provide a fundamentally improved understanding of mercury toxicity in dental auxilaries. It may also serve as a model study that can be applied to other studies of toxic metals.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 1, 1979 - August 31, 1980

TITLE: Predicting Diluted Vapor Ratios for Solvent Mixtures

PROJECT: 5 R01 OH00889-02

PRINCIPAL INVESTIGATOR & ADDRESS:

William J. Popendorf, Ph.D.
University of California
Earl Warren Hall
Berkeley, CA 94720

GRANTEE INSTITUTION: University of California

OBJECTIVE:

- To develop and verify an engineering model for the prediction of multicomponent vapor concentrations of evaporating organic solvent mixtures from the measurements of a single component of the vapor phase and quantitative analysis of the bulk liquid

METHODOLOGY:

This study uses an engineering model of the processes of evaporation and dilution to breathing zone concentrations with a thermodynamic model to predict the equilibrium vapor concentrations. The approach is a calculation of relative vapor ratios to eliminate the approximation of otherwise indeterminant mass transfer parameters, and a breakthrough in the computer prediction of the thermodynamic parameters, activity coefficient, which adjusts for non-ideal liquid behavior.

PROGRESS & ACCOMPLISHMENTS:

A computer algorithm entitled VAPRAT was developed to compute the ratio between the vapor concentrations of two or more components. The results of the study have validated the use of this mathematical model to predict the relative vapor ratios in the experimental setting. VAPRAT was shown to be considerably more accurate than the American Conference of Governmental Industrial Hygienists (ACGIH) method for mixtures.

SIGNIFICANCE TO NIOSH:

This study employs recent advances in physical chemistry as well as good engineering practices to solve a recognized problem in many industrial situations. The prediction model will be a major contribution to industrial hygiene air sampling theory and practice. The ability to predict ratios will permit more accurate estimations of vapor hazards and solvent substitutions, and potentially reduce the requirements for multiple solvent analyses.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: September 28, 1979 - August 31, 1980

TITLE: Lead--Its Renal Handling and Erythropoietin

PROJECT: 9 R01 OH00913-04

PRINCIPAL INVESTIGATOR & ADDRESS:

Arthur J. Vander, M.D.
Department of Physiology
Ann Arbor, MI 48104

GRANTEE INSTITUTION: University of Michigan

OBJECTIVES:

- To evaluate the possible role of lead, as an activator of the renin-angiotensin-aldosterone system (RAAS), in generating chronic hypertension
- To further clarify the renal mechanisms of lead-handling
- To evaluate the effect of lead on the metabolism of zinc and other trace elements

METHODOLOGY:

This investigation studied the hypertensive effects of lead, alone or in combination with other stimuli, such as psychosocial stress and cadmium exposure. The role of RAAS was evaluated using pharmacologic blockers. Clearance and stop-flow techniques in vivo were employed as well as renal slices and isolated perfused tubules in vitro.

PROGRESS & ACCOMPLISHMENTS:

The results from this investigation have shown that small doses of lead increase renal electrolyte excretion and renin secretion; and decrease renin breakdown. Moreover, small doses also produce long standing stable hypertension in rats.

This investigation has determined that lead itself is filtered, reabsorbed and secreted by the kidney. The lead transport pathway interacts with those for tin and zinc, in that tin inhibits lead uptake by renal cells, and lead inhibits the reabsorbtion of zinc.

SIGNIFICANCE TO NIOSH:

The results from this investigation will provide critical information concerning whether or not lead increases the incidence of human hypertension and the mechanisms by which it may do so. It also may reveal that subclinical zinc deficiency can be produced by moderate exposure to lead.

PUBLICATIONS RESULTING FROM THIS GRANT:

- Victory, W., Vander, A.J., Mouw, D.R.:1979: Effect of Acid Base Status on Renal Excretion and Accumulation of Lead in Dogs and Rats, American Journal of Physiology, v. 237, 398-407.
- Victory, W., Vander, A.J. Mouw, D.R.:1979: Renal Handling of Lead in Dogs, Stop-Flow Analysis, American Journal of Physiology, v. 237, 408-414.
- Fleischer, N., Mouw, D.R., Vander, A.J.:1980: Chronic Effects of Lead on Renin and Renal Sodoim Excretion, Journal of Laboratory and Clinical Medicine, v. 95, 759-770.

PERIOD COVERED: September 1, 1979 - August 31, 1980.

Other/Toxicology/Human/Cancer

TITLE: Mortality Experience of Workers Exposed to Haloethers

PROJECT: 5 R01 OH00932-02

PRINCIPAL INVESTIGATOR & ADDRESS:
Bernard S. Pasternack, Ph.D.
550 First Avenue
New York, NY 10016

GRANTEE INSTITUTION:
New York University
Medical Center

OBJECTIVES:

- To update the mortality experience of chloromethyl-methyl ether (CMME) workers in six previously studied firms for the five year period 1973-1977
- To include all exposed and nonexposed production workers in a seventh firm in the retrospective cohort for complete mortality follow up from 1955-1977
- To characterize the respiratory cancer and other mortality experience of the CMME-exposed workers according too duration and intensity of CMME exposure
- To describe the temporal patterns of respiratory cancer mortality including estimation of the induction-latency period

METHODOLOGY:

A classification scheme for ranking the magnitude of CMME exposure according to plant operation and job classification was developed, and controls from company employment files were selected. The exposure period and exposure rank on all CMME exposed and control employees at the seventh firm is being compiled and coded.

The total employment period, date of birth, race and social security number were also obtained. Deaths among ex-employees at the seven companies whose vital status is unknown were ascertained from Social Security records. Death certificates and diagnostic confirmation, where possible, are being obtained. The data will be analyzed by a combination of the person-years approach and the modified life-table method.

PROGRESS & ACCOMPLISHMENTS:

All seven chemical companies that produced chloromethyl ethers (CME) agreed to participate in the study. Data collection forms have been designed and coded. Updated coding has been completed for one firm and is in process for the other firms. The companies are providing death certificates when available. A table has been compiled indicating the changes in status between 1972 and 1979 for workers at two companies.

SIGNIFICANCE TO NIOSH:

The results of this study will help confirm existing information and will also expand the data concerning dose response relationship latency period and the risk of low level exposure.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1979 - May 31, 1980

TITLE: Atomic Spectroscopic Determination of Metals in Urine

PROJECT: 1 R01 OH01085-01

PRINCIPAL INVESTIGATOR & ADDRESS

Ramon M. Barnes, Ph.D.
Department of Chemistry
GRC Tower I
Amherst, MA 01003

GRANTEE INSTITUTION: University of Massachusetts

OBJECTIVES:

- To develop a means to screen urine samples to detect occupational trace element exposure
- To extend the resin - inductively coupled plasma (ICP) method from 10 to more than 26 elements
- To evaluate the general applicability of the technique developed
- To test the method with urine samples from patients suffering liver disorders
- To extend the method established to lower concentrations levels through improved sample handling and presentation techniques
- To evaluate with characterized urine samples at least one new chelating resin shown to have similar characterization to the present resin

METHODOLOGY:

The separation and concentration capabilities of a poly (dithiocarbamate) resin will be combined with the detection power of inductively coupled plasma - atomic emmission spectrometry for the determination of ten or more elements at ultra trace concentration levels in urine.

The resin will provide separation of analyte metals from electrolytes and organic matrix constituents in urine and will so concentrate by at least 125 times. This resin, ICP method, will be extended from 10 elements in urine to more than 26 elements known to sequester with the resin. Concentration factors of greater than 125 times will be attempted for all elements found to be sequester quantitatively from the urine sample.

The general applicability of the resin, ICP technique, will be evaluated for simultaneous, multielement analysis of urine samples for semi-routine monitoring of occupational trace element exposure. A survey of samples from patients with liver diseases will be carried out. Control samples will be analyzed by electrothermal atomization atomic absorption spectrophotometry and ICP.

best copy available

PROGRESS & ACCOMPLISHMENTS:

This is a new grant. Progress and accomplishments will be reported in the FY 81 grant report.

SIGNIFICANCE TO NIOSH:

The determination of trace and ultratrace elements in urine may improve clinical and medical diagnosis and treatment in humans. The approach used in this investigation may lead to comprehensive monitoring and control of occupational trace element exposure.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date.

PERIOD COVERED: August 1, 1980 - July 31, 1981

blank page

OTHER NIOSH GRANT PROGRAMS

blank page

DEMONSTRATION PROGRAMS FOR SAFE ASBESTOS REMOVAL IN SCHOOLS

Asbestos previously used in the construction of school buildings has been the subject of much concern over its possible health hazards to exposed school children. It has been recommended by the Environmental Protection Agency (EPA) that corrective action (asbestos removal, encapsulation or enclosure) be taken to prevent this exposure. It is imperative that school officials and other responsible state and local officials, do not endanger the health of the workers conducting these corrective actions when attempting to comply with EPA's recommendation. This will require that contracts awarded for asbestos removal, encapsulation or enclosure include provisions requiring the contractor to use safe techniques, including complying with appropriate regulations of the Occupational Safety and Health Administration (OSHA) and EPA.

NIOSH with $450,179 from the National Cancer Institute awarded demonstration grants in Fiscal Year 1980 to seven universities and state and local health and education agencies for development of demonstration programs for the dissemination of information about accepted procedures for safe removal, encapsulation, or enclosure of deteriorated asbestos previously used in the construction of schools.

Such procedures include the proper work-site isolation, ventilation, respirators, protective clothing and safe disposal of the asbestos which has been removed. OSHA regulations governing workplace exposure to asbestos are to be followed.

Target audiences include state and local school and health officials, contractors and their employees and school maintenance personnel.

Information to be disseminated about accepted procedures would be similar to those presented in EPA guidelines and NIOSH manuals.

Methods for dissemination include motion pictures, other audio-visual aids, written materials, demonstration models or other methods which may seem appropriate. Actual asbestos removal or treatment is not supported. Study design includes a plan for evaluation of the effectiveness of this information transfer.

TITLE: Asbestos Removal or Treatment in Oklahoma Schools

PROJECT: 1 R18 OH01049-01

PRINCIPAL INVESTIGATOR & ADDRESS:
Bob Martin
2500 N. Lincoln
Oklahoma City, OK 73105

GRANTEE INSTITUTION:
Oklahoma State Department
of Education

OBJECTIVES:

- To increase awareness of Enviromental Protection Agency(EPA) guidelines and Occupational Safety and Health Administration (OSHA) regulations governing asbestos by school officials, architects and contractors involved in asbestos corrective programs
- To provide school districts with the technical information they need to establish or improve their corrective programs

METHODOLOGY:

A series of highly publicized asbestos workshops was presented in public school districts throughout the state. This investigation will provide for the effective dissemination of information about accepted procedures for safe removal, encapsulation or enclosure of deteriorated asbestos previously used in the contruction of schools in Oklahoma. Specialized technical assistance will be provided to interested participants. Specific tasks during the project include:

- Identifying appropriate procedures for dealing with various asbestos problems
- Packaging the assembled information for presentation in demonstration workshops; conducting a test workshop for the potential target audience
- Presenting 10 asbestos demonstration workshops on a county or regional basis with emphasis on audiovisual presentation
- Conducting a publicity campaign and providing technical assistance in the form of an asbestos hotline
- Forwarding relevant technical information
- Response to technical questions
- Providing on-site assistance as needed

PROGRESS & ACCOMPLISHMENTS:

Six regional asbestos workshops have been presented in Oklahoma by the State Department of Education, The State Health Department and EPA. The major thrusts of the workshops were to present the current proposed regulations from EPA, a review of the current OSHA regulations and a detailed discussion of the alternative corrective action. In addition, various materials were reproduced for the workshops. These materials covered such subjects as available disposal sites, asbestos contractors, resource personnel and government publications.

SIGNIFICANCE TO NIOSH:

It is expected that a large percentage of Oklahoma school officials will become increasingly aware of the potential sources of exposure to asbestos in school buildings. This is extremely important since any exposure to asbestos probably carries some risk of disease. Once detected, school asbestos hazards must be corrected. This program will provide step-by-step procedures for initiating corrective actions which should produce the least possible hazard to workers and also minimize the degree of contaminaion of the school building.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1980 - May 31, 1981

TITLE: Safe Asbestos Removal or Treatment in Schools

PROJECT: 1 R18 OH01050-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Henry Anderson, M.D.
Dept. of Health &
Social Services
1 West Wilson Street
Madison, Wisconsin 53702

GRANTEE INSTITUTION:

Wisconsin Department of
Health & Social Services

OBJECTIVES:

- To insure that workers, contractors, and building officials dealing with indoor asbestos problems are fully aware of asbestos hazards
- To insure that this knowledge is translated into appropriate actions which prevent worker and building user exposure to asbestos

METHODOLOGY:

Six symposia will be held for workers across the state of Wisconsin, which will cover the hazards, regulations, and work practices required when removing asbestos material. Five symposia will be held for building managers. In addition, the current Wisconsin Program of Asbestos will be monitored.

A data processing/tracking system will be developed for building hazard investigations. Actual work-site activities will be examined, and air samples will be taken and quantified.

PROGRESS & ACCOMPLISHMENTS:

Work has begun on the computerization of data collected prior to the grant award. A followup program has been instituted to monitor the effectiveness of corrective actions taken by schools. Educational materials directed at contractors, architects, engineers, and school building officials are being developed.

SIGNIFICANCE TO NIOSH:

This project constitutes a model statewide surveillance system, and contains a follow-up evaluation of recommendations concerning the removal of asbestos.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1980 - May 31, 1981

TITLE: Development For Controlling Asbestos in Buildings

PROJECT: 1 R18 OH01052-01

PRINCIPAL INVESTIGATOR & ADDRESS:

J. Maichle Bacon, M.P.H.
401 Division Street
Rockford, IL 61108

GRANTEE INSTITUTION: Winnebago County Department of Public Health

OBJECTIVE:

- To increase the awareness level needed to assure all corrective actions involving asbestos-containing surface materials, and adherence to recommended procedures and safety precautions

METHODOLOGY:

A lecture series and educational materials targeted at key groups which have decision making, monitoring, enforcement, maintenance or active corrective type roles in schools and other structures which might contain asbestos is being developed. On-going reinforcement during the course of the project is the responsibility of a specifically trained local interdisciplinary panel.

PROGRESS & ACCOMPLISHMENTS:

A health educator has been hired and the selection of the interdisciplinary panel has been completed.

SIGNIFICANCE TO NIOSH:

This research is unique in its development of local resources to ensure proper and thorough asbestos control efforts in the schools. The use of a local public health department in encouraging resource development is a possible approach to ensuring adequate coverage nationally.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1979 - May 31, 1980

TITLE: Safe Asbestos Treatment Program

PROJECT: 1 R18 OH01053-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Roy Buchan, D.P.H.
110 Vet Science Building
Fort Collins, CO 80523

GRANTEE INSTITUTION: Colorado State University

OBJECTIVE:

- To provide training and technical assistance to state and local schools and health officials, school maintenance personnel, contractors, and construction workers which will facilitate:
  - The recognition of potential asbestos related problems
  - The selection of appropriate treatment process(es)
  - The implementation of selected treatment process(es)
  - The final resolution of identified asbestos related problems

METHODOLOGY:

This project will provide educational forums, and personalized technical assistance and resource materials in order to encourage the development and implementation of skills and procedures required for the safe control or removal of asbestos in Colorado schools. Specific program strategies are targeted to the public school community and the construction industry.

PROGRESS & ACCOMPLISHMENTS:

Project staff have identified school districts, personnel, and facilities within Colorado, and such information has been stratified for random sampling and initiation of program field activities. Contacts have been made with key education officials, the Associated General Contractors of Colorado, and the AFL-CIO building and Construction Trades Personnel relative to training activities and appropriate training modes.

SIGNIFICANCE TO NIOSH:

This project emphasizes the enhancement of participant capabilities for making informed decisions concerning the safe and appropriate removal of asbestos.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1980 - May 31, 1981

TITLE: Missouri Workshops on Asbestos Treatment in Schools

PROJECT: 1 R18 OH01054-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Louis V. Holroyd, Ph.D.
215 University Hall
Columbia, MO 65211

GRANTEE INSTITUTION: University of Missouri

OBJECTIVES:

- To provide training in the safe removal or encasement of asbestos to school officials, contractors and other workers involved in asbestos corrective programs in Federal Region VII
- To review State and Federal regulations on asbestos removal and encasement for participants
- To appraise participants of recent research findings in the areas of asbestos removal or treatment
- To familiarize participants with equipment needed to safely remove or treat asbestos
- To demonstrate problems and solutions first hand through site visits to a local school

METHODOLOGY:

One day seminars will be conducted at four Missouri locations: Columbia, Rolla, St. Louis and Kansas City. The first workshops will be a prototype production at Columbia and will be open to school administrators, (as interested), contractors, and workers. Later, workshops at the same location will be open to similar groups both in and out of state.

Specific plans for the prototype removal project will be formulated. Removal work will be completed and lessons and corresponding tapes will be made and edited. The first workshop will be conducted after the removal work has been completed. An evaluation of the entire project will be performed after all sessions are completed.

The workshop activities will be part of the university's engineering extension programs. some specific training aids needed for the workshops will be distributed to concerned individuals.

PROGRESS & ACCOMPLISHMENTS:

Investigators have made an extensive review of audiovisual materials. Some lesson plans have been completed and the remainder is being prepared. Plans are progressing for the first workshop which will be held shortly.

SIGNIFICANCE TO NIOSH:

Through this project, a mechanism will be established for the development of workshops to train and demonstrate the safe removal of asbestos materials. The approach to training and information dissemination may serve as a model program. As a training program, it sets an example for initiating such a program in a new geographical region.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1980 - May 31, 1981

TITLE: School Asbestos Fund for Removal

PROJECT: 1 R18 OH01062-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Melvin K. Koizumi
Department of Health
1250 Punchbowl Street
Honolulu, HA 96813

GRANTEE INSTITUTION: State of Hawaii

OBJECTIVES:

- To provide workshop training of state and local officials and contractors in proper, accepted procedures for safe removal and encapsulation of asbestos material
- To establish a program of air-sample monitoring and analyses to provide data on contractor compliance with Environmental Protection Agency (EPA) and/or Occupational Safety and Health Administration (OSHA), on preventive containment measures, and on corrective activity effectiveness
- Provide on-site surveillance and inspection of actual work activities to ensure compliance with contract specifications

METHODOLOGY:

A resource base will be established by gathering information from NIOSH, EPA, and other sources in order to develop audio visual aids for workshop use and on-site demonstrations. Presentations will involve films and/or slide presentions, demonstration models, and printed materials.

Inspectors will be hired to monitor daily activities through the gathering of air-sampling data. Air samples will be analyzed and cataloged by a certified laboratory using phase microscopy.

Inspectors taking daily air samples will also have the responsibility of over-seeing the encapsulation activities.

PROGRESS & ACCOMPLISHMENTS:

Plans for implementation have been initiated and some training sessions have been scheduled.

SIGNIFICANCE TO NIOSH:

This project may result in an increased awareness of asbestos hazards and will disseminate information to contractors of proper abatement techniques.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1980 - May 31, 1981

TITLE: Asbestos Removal in Schools

PROJECT: 1 R18 OH01072-01

PRINCIPAL INVESTIGATOR & ADDRESS:

Anthony McMahon
Dept. of Environmental
Protection
John Fitch Plaza
Trenton, NJ 08625

GRANTEE INSTITUTION: State of New Jersey

OBJECTIVE:

- To conduct tests of an innovative asbestos removal procedure to determine its effectiveness, versatility, cost and safety

METHODOLOGY:

Three school sites in New Jersey will be selected for field tests of the proposed removal system. The asbestos containing material, which is to be scraped from the coated interior surfaces using a specially designed attachment, will fall directly into hoppers. The removed asbestos materials will then be drawn through a hose to a remotely located vacuum loader truck where asbestos containing particulate matter will be removed from the air stream, prior to exhaust, by a bag filtering system. Both wet and dry surface preparation will be tested. The removed asbestos materials will be withdrawn from the vacuum loader truck via an auger, through an off loading port, and sprayed with water just prior to entering barrels containing 6 mil plastic bags. During the removal process, a representative member of ambient and worker respiratory-zone air samples will be collected on nucleopore membrane filters and analyzed for their asbestos content, using electron microscopy techniques. A cost analysis of the removal technique will also be performed.

PROGRESS & ACCOMPLISHMENTS:

Investigators have been involved primarily in the location of schools which meet the criteria for asbestos content and friability.

SIGNIFICANCE TO NIOSH:

This project will provide an evaluation of an asbestos removal system, as well as reduce health hazards to school children. The results of this project will aid the development of regulations and guidelines covering asbestos removed under the Toxic Substances Control Act and the National Emission Standards for Hazardous Air Pollutants.

PUBLICATIONS RESULTING FROM THIS GRANT: None to date

PERIOD COVERED: June 1, 1980 - May 31, 1981

blank page

HEALTH HAZARD EVALUATION COOPERATIVE AGREEMENTS

The National Institute for Occupational Safety and Health (NIOSH) has established cooperative agreements with two universities to test whether non-federal organizations can successfully perform health hazard evaluations.

The Harvard University and the University of North Carolina each received approximately $300,000 in Fiscal Year 1980 from NIOSH for the first of two years of these pilot projects. NIOSH will assign select health hazard evaluation requests to these universities and will assist them in organizing and managing their programs.

These health hazard evaluations have as their purpose the study of places of employment to determine whether susbstances found there have potentially toxic effects in concentrations as used or found in the workplace.

These projects are intended ultimately to increase the number of states, universities, and other non-profit institutions capable of assisting employers and employees in recognizing and controlling occupational hazards.

SURVEILLANCE COOPERATIVE AGREEMENTS

NIOSH intends to establish programs, which will promulgate information on potentially toxic substances or harmful physical agents as it relates to the high incidence of occupational illnesses, as one of its research goals. In addition, NIOSH is developing a national occupational health surveillance system that will make it possible to monitor changes in the nature and magnitude of workplace related diseases. In order to accomplish this task, NIOSH has identified a surveillance strategy which has two main elements:

- The development of a national information base would identify potential health hazards in the workplace. This base would have as its main goals the identification of types of industries, occupational groups and trade name and generic hazards found in the workplace. Also involved would be the dissemination of information about these hazards to government agencies, researchers, workers and their representatives, employers and medical care providers.

- The development of nationwide information systems would have as their goal the early detection of occupational disease. Such systems would detect trends and possible determinants of occupationally related disease and would develop, maintain and analyze the information, adapting existing national, State and other health data systems.

Long range plans call for such a national occupational health surveillance network to include a health hazard information and identification system. This information system would be used by State epidemiologists or other medical care providers in the same way that information from Poison Control Centers in now made available to the medical community.

To develop a national occupational health surveillance network as rapidly as possible, it is necessary to utilize existing State health data systems. Although some of the NIOSH health surveillance needs can be met by using existing national health data systems, many needs, such as the monitoring of reportable occupational diseases and determination of the incidence and prevalence of occupation-related disease, presently cannot be addressed.

This pilot program seeks to develop, at the State level, four occupational health surveillance systems by adapting or expanding existing State health data systems. Ultimately, this program could be expanded to include all fifty States. A suitable system would include information that is adequate in quantity and quality and provide a basis for systematic analysis and evaluation.

TITLE: Demonstration Of Occupational Health Surveillance

PROJECT: 1 U01 OH01213-01

PROJECT DIRECTOR:	Bruce C. Kelley, Ph.D.
RECIPIENT INSTITUTION:	Rhode Island Department of Health

DESCRIPTION:

Rhode Island's occupational health surveillance project proposes to develop an occupational health surveillance model, to determine tis utility to states and the nation as a whole, and to demonstrate its effectiveness in the allocation of occupational health service resources. Activities in 1981 and 1982 will concentrate on the use of mortality and morbidity data files. The latter includes information derived from hospital discharges, disability insurance, and worker's compensation data files. NIOSH will collaborate with the recipient in the developmental and analytical phases of the project. Specifically, NIOSH's contribution in 1981 will include the training of state personnel in occupational and industry coding, the adaptation of nationally-derived population estimates for purposes of calculating standard mortality ratios and the adaptation of a sentinel health event model on the surveillance of occupation-related mortality and morbidity.

TITLE: Utah Occupational Health Surveillance Project

PROJECT: 1 U01 OH01207-01

PROJECT DIRECTOR:	John E. Brockert
RECIPIENT INSTITUTION:	Utah State Department of Health

DESCRIPTION:

Utah's occupational health surveillance project proposes to develop a surveillance system that captures appropriate data on occupation-related morbidity and mortality and provides for its systematic analysis and evaluation. Activities in 1981 and 1982 will concentrate on the use of mortality (death and fetal death), birth, and morbidity (Bureau of Labor Statistics Supplementary Data Systems) data to facilitate the systematic analysis of occupation-related morbidity, mortality, and fetal outcomes. NIOSH will collaborate with the recipient in the developmental and analytical phases of the project. Specifically, NIOSH's contribution in 1981 will include the training of state personnel in occupation and industry coding and the adaptation of a sentinel health event model in the surveillance of occupation-related morbidity and mortality.

TITLE: Maine Occupational Health Surveillance Project

PROJECT: 1 U01 OH01184-01

PROJECT DIRECTOR:	Ellen M. Naor
RECIPIENT INSTITUTION:	Maine Department of Human Services

DESCRIPTION:

Maine's occupational health surveillance project has two principal goals: To provide more useful information for the detection of occupational health hazards and disease and to demonstrate an effective process for adapting existing state data systems for use in detecting occupational health problems. Activities in 1981 and 1982 will concentrate on the use of mortality (death records) and morbidity (hospital discharge, Occupational Safety and Health Administration Form 200-S, etc.) data for purposes of occupational health surveillance. NIOSH will collaborate with the recipient in the developmental and analytical phases of the project. Specifically NIOSH's contribution in 1981 will include the training of state personnel in occupation and industry coding, as well as the adaptation of nationally-derived population estimates for purposes of calculating standard mortality ratios.

TITLE: Occupational Health Surveillance System

PROJECT: 1 U01 OH01165-01

PROJECT DIRECTOR:	Vito M. Logrillo
RECIPIENT INSTITUTION:	New York Department of Health

DESCRIPTION:

New York's occupational health surveillance project proposes to utilize the Vital Records Registration of the state as a basis to develop an occupational health surveillance capability. Activities in 1981 and 1982 will concentrate on supplementing existing mortality (death and fetal death) and birth files to facilitate the systematic analysis of occupation-related mortality and fetal outcomes. NIOSH will collaborate with the recipient in the developmental and analytical phases of the project. Specifically, NIOSH's contribution in 1981 will include the training of state personnel in occupation and industry coding. In addition, NIOSH will assist the recipient in the adaptation of a sentinel health event model in the surveillance of occupation-related fetal outcomes.

Research Grants Program-Status
September 1980

Initiative Area	Competing and Non-Competing Grants Awarded	Active Grants FY80 Total Award	
Asbestos	2	$181,640	
Asbestos in Schools Demonstrations	7	450,179	(NCI)
Behavioral and Neurotoxicity	10	1,158,005	
Cancer	5	629,176	
Cardiovascular Disease	2	181,434	
Chronic Effects of Trauma	4	415,088	
Control Technology	8	522,942	
Dermatology	7	624,829	
	1	114,694	(EPA)
Digestive Disease	1	57,999	
Energy	1	99,109	
Mining	2	83,919	(EPA)
Other	14	1,137,575	
Physical Agents	9	811,960	
Protective Equip.	3	184,575	
Radiation	1	220,291	(EPA)
Reproduction	5	381,951	
Respiratory	7	488,293	
Safety	3	165,424	
Sidestream Smoking	0		
Total	81	$7,040,000 $450,179 $418,904	NIOSH NCI EPA

Research Grants Program-Status
September 1984

TITLE: Maine Occupational Health Surveillance Project

PROJECT: [illegible]

Active Grants from Total Award

Competing and Non-Competing Grants Awarded

[illegible]

Maine Department of Human Services

[illegible]

Maine's Occupational Health Surveillance [illegible]

[illegible]

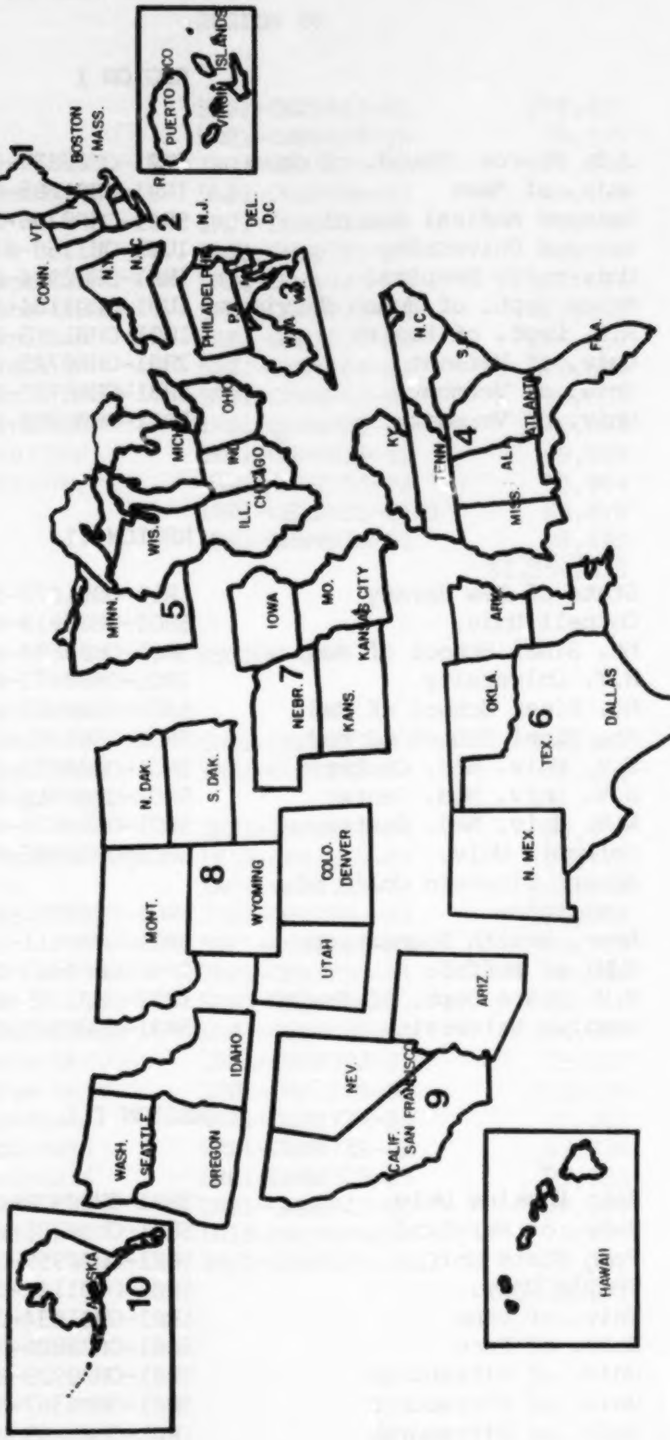
TITLE: [illegible]

PROJECT: [illegible]

PROJECT DIRECTOR: [illegible]

[illegible]

STATES AND REGIONS


1
BOSTON
MASS.
CONN.
VT.
R.I.
PUERTO RICO
VIRGIN ISLANDS
2
N.Y.
N.J.
DEL.
D.C.
3
PHILADELPHIA
PA.
W.VA.
4
N.C.
S.C.
ATLANTA
FLA.
KY.
TENN.
AL.
MISS.
5
MICH.
OHIO
IND.
CHICAGO
ILL.
WIS.
MINN.
6
ARK.
LA.
OKLA.
TEX.
DALLAS
N. MEX.
7
IOWA
MO.
KANSAS CITY
NEBR.
KANS.
8
N. DAK.
S. DAK.
MONT.
WYOMING
COLO.
DENVER
UTAH
9
ARIZ.
NEV.
CALIF.
SAN FRANCISCO
HAWAII
10
IDAHO
WASH.
SEATTLE
OREGON
ALASKA

RESEARCH AND DEVELOPMENT GRANTS BY

STATES AND REGIONS

REGION I

J.B. Pierce Found. of Conn	5R01-OH00836-02	$81,839
Univ. of Mass	1R01-OH01085-01	52,925
Harvard Medical School	5R01-OH00706-03	112,168
Harvard University	1U01-OH1168-01	299,999
University Hospital	1R01-OH00984-01	129,117
Maine Dept. of Human Services	1U01-OH01184-01	61,031
R.I. Dept. of Health	1U01-OH01213-01	64,974
Univ. of Vermont	2R01-OH00745-03	237,729
Univ. of Vermont	3R01-OH00745-0252	33,805
Univ. of Vermont	5R01-OH00888-02	96,023
		$1,169,610

REGION II

State of New Jersey	1R18-OH01072-01	$110,000
Cornell Univ.	5R01-OH00910-02	81,193
Mt. Sinai School of Med.	5R01-OH00690-04	24,579
N.Y. University	1R01-OH00973-01	120,093
Mt. Sinai School of Med.	5R01-OH00682-03	85,617
Mt. Sinai School of Med.	5R01-OH00681-01	96,934
N.Y. Univ. Med. Center	5R01-OH00932-02	53,326
N.Y. Univ. Med. Center	5R01-OH00915-02	94,095
N.Y. Univ. Med. Center	5R01-OH00678-02	126,928
Columbia Univ.	5R01-OH00906-02	113,695
Albert Einstein Coll. of Medicine	1R01-OH00851-01	151,077
Amer. Health Foundation	5R01-OH00611-05	91,577
SUNY at Buffalo	1R01-OH00923-01	26,497
N.Y. State Dept. of Health	1U01-OH01165-01	89,778
Yeshiva University	5R01-OH00535-05	113,688
		$1,379,077

REGION III

John Hopkins Univ.	5R01-OH00920-02	$110,422
Univ. of Maryland	5R01-Oh00735-03	45,611
Penn State Univ.	5R01-OH00959-02	42,278
Temple Univ.	1R01-OH01119-01	145,471
Univ. of Penn	1R01-OH01034-01	133,675
Univ. of Penn	5R01-OH00886-02	218,708
Univ. of Pittsburgh	5R01-OH00929-02	220,291
Univ. of Pittsburgh	5R01-OH00367-09	47,830
Univ. of Pittsburgh	1R01-OH00865-01	72,710
		$1,036,996

RESEARCH AND DEVELOPMENT GRANTS BY STATES AND REGIONS

REGION IV

Univ. of Alabama	5R01-OH00912-02	$78,615
Univ. of Florida	5R01-OH00316-15	79,275
Emory University	1R01-OH01124-01	113,581
University of Kentucky	5R01-OH00849-02	44,109
Duke University	5R01-OH00823-02	92,470
Duke University	5R01-OH00781-03	52,388
North Carolina State Univ.	5R01-OH00744-02	131,615
North Carolina State Univ.	5R01-OH00933-01	221,896
Univ. of North Carolina	5R01-OH01023-01	66,957
Univ. of North Carolina	5R01-OH01164-01	300,600
Univ. of North Carolina	5R01-OH00953-01	99,863
Univ. of North Carolina	1R01-OH00905-01	76,093
Univ. of South Carolina	5R01-OH00838-02	49,929
Univ. of South Carolina	5R01-OH00954-01	53,864
Vanderbilt Univ.	1R01-OH00895-01A1	65,078
Vanderbilt Univ.	1R01-OH00972-01	28,490
		$1,554,823

REGION V

American Dental Assoc.	5R01-OH00742-03	$38,940
Illinois Instit. of Tech.	5R01-OH00917-02	72,154
Univ. of Illinois Chicago Circle	2R01-OH00514-06	89,735
Winnebago County Health Dept.	1R18-OH01052-01	22,777
Henry Ford Hospital	5R01-OH00705-02	160,988
Regents of Univ. of Mich.	2R01-OH00707-04	106,988
Univ. of Michigan	5R01-OH00913-05	84,706
Univ. of Michigan	7R01-OH01253-01	98,796
Univ. of Minnesota	5R01-OH00876-02	68,718
Univ. of Minn. Med. School	5R01-OH00631-04	134,573
Case Western Reserve Univ.	1R01-OH00992-01	51,815
Case Western Reserve Univ.	1R01-OH01149-01	114,694
University of Cincinnati	5R01-OH00774-03	37,367
University of Cincinnati	5R01-OH00739-02	43,838
University of Cincinnati	5R01-OH00773-03	99,355
St. Luke's Hospital	1R01-OH00947-01	99,109
Wisc. Dept. of Health	1R18-OH1050-01	79,726
Univ. of Michigan	3R01-OH00679-0451	18,331
		$1,422,111

REGION VI

Univ. of Arkansas	1R01-OH00952-01	$126,176
Louisiana State Univ.	5R01-OH00835-02	31,925
Okla State Dept. of Educa.	1R18-OH01049-01	53,192
Univ. of Texas Med. Br. Galvest.	5R01-OH00897-02	67,739
Univ. of Texas Dallas	1R01-OH01152-01	85,196
Texas Tech. Univ.	5R01-OH00798-03	35,488
		$399,716

REGION VII

Univ. of Iowa	5R01-OH00825-02	$78,863
Iowa State Univ.	1R01-OH00859-01	000
Kansas State Univ.	5R01-OH00874-02	98,026
Univ. Of Missouri	1R18-OH01054-01	41,902
Univ. of Missouri	1R01-OH00986-01	57,999
Univ. of Nebraska	1R01-OH01029-01	25,071
		$301,861

REGION VIII

Colorado School of Mines	5R01-OH00822-02	$73,921
Colorado State University	1R18-OH01053-01	93,836
Utah State Dept. of Health	1U01-OH01207-01	65,855
		$233,642

REGION IX

Arizona State Univ.	1R01-OH00969-01	$63,494
Univ. of Arizona	5R01-OH00860-02	48,598
City of Hope Med. Center	5R01-OH00914-02	308,503
Regents of Univ. of Calif.	5R01-OH00889-02	30,036
Stanford University	1R01-OH00991-01	9,998
The Aerospace Corp.	1R01-OH01030-01	67,423
Univ. of California	1R01-OH01004-01	37,199
" " "	5R01-OH00404-06	57,821
" " "	2R01-OH00714-04	78,635
" " "	5R01-OH00896-07	73,053
" " "	5R01-OH00858-02	57,821
" " "	1R01-OH01108-01	66,966
Stanford University	1R01-OH00978-01	128,326
Univ. of California	5R01-OH00766-02	57,771
State of Hawaii Dept.	1R18-OH01062-01	48,746
		$1,134,088

INDEX OF PRINCIPAL INVESTIGATORS

Page

Abou-Donia, Mohamed B., Ph.D. 36
Alarie, Yves C., Ph.D. 143
Anderson, Henry, M.D. 192
Armstrong, Thomas, Ph.D. 64
Bacon, J. Maichle, M.P.H. 198
Barker, Roger L., Ph.D. 123
Barnes, Ramon M., Ph.D. 188
Baum, Gerald L., M.D. 154
Bernstein, Leonard I., M.D. 85
Bialik, Ora, Ph.D. 138
Bickers, David B., M.D. 94
Brockert, John E. 209
Buchan, Roy, D.P.H. 199
Burg, William R., Ph.D. 156
Burrell, Robert, Ph.D. 139
Caruso, Joseph A., Ph.D. 173
Carr, Peter W., Ph.D. 179
Cohen, Ellis N., M.D. 133
Craighead, John E., M.D. 149
Dews, Peter B., M.D. 32
Donham, Kelley J., D.V.M. 158
Drinkwater, Barbara, Ph.D. 107, 111
Emerson, Paul 112
Evans, Hugh L., Ph.D. 44
Fanslow, Glenn E., Ph.D. 176
Feigley, Charles E., Ph.D. 72
Feldman, Robert G., M.D. 45
Fine, Lawrence J., M.D. 136
Frymoyer, John, M.D. 66
Gellin, Gerald A., M.D. 83
Goldsmith, Werner, Ph.D. 121
Gonzalez, Richard, Ph.D. 104
Halberg, Franz, M.D. 30
Hart, Franklin D., Ph.D. 75
Heinsohn, Robert F., Ph.D. 76
Henderson, Donald, Ph.D. 106, 116
Hersh, Solomon P., Ph.D. 69
Hewitt, William, Ph.D. 95
Holroyd, Louis V., Ph.D. 200
Houten, Lorne, Ph.D. 55
Hulka, Barbara, M.D., M.P.H. 89
Humes, Larry E., Ph.D. 110, 114
Johnson, Arthur T., Ph.D. 119
Karasek, Robert A., Ph.D. 59
Karis, Joannes H., M.D. 174
Karol, Meryl H., Ph.D. 177
Kelley, Bruce C., Ph.D. 209

Kindwall, Eric P., M.D. 97
Koizumi Melvin K. 202
Komaki, Judi, Ph.D. 165
Konz, Stephen A., Ph.D. 108
Langolf, Gary D., Ph.D. 34
Leibman, Kenneth C., Ph.D. 171
Lippman, Morton, Ph.D. 152
Logrillo, Vito M. 210
Mancuso, Thomas F., M.D., M.P.H. 125
Martin, Bob 195
Matanoski, Genevieve M., M.D., Ph.D. 54
McMahon, Anthony 203
Meigs, J. Wister, M.D. 50
Middleman, Stanley, D. Eng. 77
Mittman, Charles, M.D. 51
Mossman, Brooke T., M.D., Ph.D. 23
Muramoto, Hiroshi, Ph.D. 74
Naor, Ellen M. 210
Nahum, Alan M., M.D. 163
Nechay, Bohdan R., D.V.M. 57
Neilsen, Donald W., Ph.D. 102
Nicholson, William, Ph.D. 49
Pasternack, Bernard S., Ph.D. 53, 186
Popendorf, William J., Ph.D. 183
Puhvel, S. Madli, M.D. 91
Rietschel, Robert L., M.D. 93
Riley, Michael, Ph.D. 115
Ross, Ira J., Ph.D. 167
Scheving, Lawrence, Ph.D. 42
Schowengerdt, Franklin D., Ph.D.
Schultz, Albert B., Ph.D. 61
Selikoff, Irving, M.D. 22
Shapiro, Irving, Ph.D. 181
Shaw, Milton C., Sc.D. 169
Shmunes, Edward, M.D. 87
Slavin, Raymond G., M.D. 145
Spencer, Peter S., Ph.D. 27, 38
Stolwijk, Jan A., Ph.D. 21
Suzuki, Yasunosuke, M.D. 153
Swartz, William J., Ph.D. 134
Tepas, Donald I., Ph.D. 40
Trudell, James, Ph.D. 147
Urback, Frederick, M.D. 92
Vander, Arthur J., M.D. 184
Verrusio, Carl A., Ph.D. 131
Ward, Wallace Dixon, Ph.D.
Weisbuger, John H., Ph.D. 47
Whittemore, Alice S., Ph.D.
Willeke, Klaus, Ph.D. 71
Yu, C.P., Ph.D. 160

INDEX OF GRANTEE INSTITUTIONS

Page

Albert Einstein College of Medicine 27, 38
American Dental Association Health Foundation 131
American Health Foundation 47
Arizona State University 169
Boston University, University Hospital 45
Case Western Reserve University 94
City of Hope Medical Center 51
Chaim Sheba Medical Center 154
Colorado School of Mines 99
Colorado State University 199
Columbia University 59
Cornell University 123
Duke University 174
Duke University Medical Center 36
Emory University 93
Georgia Institute of Technology 165
Harvard Medical School 32
Henry Ford Hospital 102
Illinois Institute of 40
Iowa State Universtiy 176
John B. Pierce Foundation Laboratory 21
John Hopkins University 54
Kansas State University 108
Louisiana State University 134
Maine Department of Human Services 210
Medical College of Wisconsin 97
Mt. Sinai School of Medicine 22, 153
Mt. Sinai School of Medicine - CUNY 49
New York Department of Health 210
New York University 152
New York University Medical Center 44, 53, 186
North Carolina State University 69, 75
North Carolina State University at Raleigh 112
Oklahoma State Department of Education 195
Pennsylvania State University 76
Research Foundation of SUNY 160
Rhode Island Department of Health 209
St. Louis University School of Medicine 145
Stanford University 133, 142
Stanford University School of Medicine 100
State of Hawaii 202
State of New Jersey 203
Temple University of Medicine 92
University of Arizona 74
University of Arkansas 42

INDEX OF GRANTEE INSTITUTIONS

University of California 77, 91, 107, 111, 121, 183
University of California - San Francisco 83
University of California - The Regents of the University of California at San Diego 163
University of Cincinnati 71, 156, 173
University of Cincinnati Medical Center 85
University of Florida 171
University of Illinois 61
University of Iowa 158
University of Kentucky 167
University of Maryland 119
University of Massachusetts 188
University of Michigan 34, 64, 136, 184
University of Minnesota 101, 179
University of Minnesota Medical School 30
University of Missouri 200
University of Missouri - Columbia 95
University of Nebraska 115
University of North Carolina 89
University of Pennsylvania 55, 138, 181
University of Pittsburgh 125, 143, 177
University of South Carolina 72, 87
University of Texas, Collier Center for Communicative Disorders 106, 116
University of Texas Medical Branch 57
University of Vermont 23, 66, 149
Utah State Deparment of Health 209
Vanderbilt University 110, 114
West Virginia University 139
Winnebago County Department of Public Health 198
Wisconsin Department of Health and Social Services 192
Yale University School of Medicine 50, 104

NIOSH ANNUAL GRANTS REPORTS-FY 80
KEY WORD INDEX

EMPHASIS AREA	KEY WORDS	PAGE
Asbestos and Asbestos Substitutes		
	Animal	22
	Administrative Methods	195, 197, 198, 199 200, 202, 203
	Analytical Methods Development	21
	Cancer	23
	Clinical	27
	Engineering	21
	Epidemiology	22
	Human	22, 195, 27
	Sampling Methods	203
	Surveillance	22, 195, 198
	Toxicology	23, 27
Behavioral and Neurotoxic Effects		
	Animal	27, 30, 32, 36, 38, 42, 44
	Cancer	42
	Clinical	27, 40, 45
	Human	27, 34, 40
	In Vitro	27, 34, 36

EMPHASIS AREA	KEY WORDS	PAGE
Behavioral and Neurotoxic Effects (Cont'd)		
	In Vivo	30, 44, 45
	Physical Agents	44
	Toxicology	27, 32, 34, 36, 38, 42
Cancer		
	Animals	47
	Epidemiology	49, 50, 53, 54, 55
	Human	49, 50, 51, 54
	In Vivo	47, 49
	Repiratory Diseases	51
	Sampling Methods	51
	Testing	55
	Toxicology	47, 49
Cardiovascular Diseases		
	Animals	47
	Epidemiology	59
	In Vitro	57
	In Vivo	57
	Toxicology	57

EMPHASIS AREA	KEY WORDS	PAGE
Chronic Effects of Trauma		
	Analytical Methods	64
	Clinical	61, 66
	Engineering Controls	64
	Human Subjects	61, 64, 66
	In Vivo	61
	Sampling	64, 66
Control Technology		
	Engineering Controls	71, 76
	Engineering Controls Devlopment	69, 72, 75, 77
	Epidemiology	74
	Ergonomics	71
	Safety	76
	Testing	76
Dermatology		
	Animals	83, 85, 91 93, 94
	Cancer	89
	Clinical Study	87, 89
	Epidemiology	87
	Human	92, 93, 94

EMPHASIS AREA	KEY WORDS	PAGE
Dermatology (Cond't)		
	In Vitro	83, 85, 91, 99
	In Vivo	83, 91, 92
	Physical Agents	91, 94
	Toxicology	83, 96
Digestive Diseases		
	Animal	95
	In Vitro	95
	Toxicology	95
Energy		
	Analytical Methods	97
	In Vitro	97
Mining		
	Cancer	100
	Epidemiology	100
	Human	100
	Sampling Methods	99
	Surveillance	99

EMPHASIS AREA	KEY WORDS	PAGE
Physical Agents		
	Administrative Methods	106
	Animal	102, 116
	Clinical	104, 111
	Controls	101
	Control Technology	107
	Engineering Control	110, 114
	Ergonomics	108, 112
	Human	101, 102, 104, 107, 108, 111, 115
	Job Design	108, 112
	In Vitro	102
	In Vivo	104, 111, 115, 116
	Testing	110, 114
Protective Equipment		
	Administrative Methods	121
	Asbestos	123
	Asbestos Substitutes	123
	Human	119
	In Vivo	119
	Testing	123

EMPHASIS AREA	KEY WORDS	PAGE
Radiation		
	Cancer	125
	Epidemiology	125
	Human	125
Reproductive Effects		
	Animal	131, 134
	Cancer	136
	Clinical Studies	131
	Epidemiology	133, 138
	Human	136
	In Vitro	131
	In Vivo	131, 134
	Physical Agents	133, 134, 136, 138
	Sampling Methods	133
	Toxicology	131, 134
Respiratory Diseases		
	Analytical Methods	160
	Animal	139, 143, 145, 147, 149, 152 153, 158
	Cancer	153, 156
	Clinical Studies	154, 158
	Epidemiology	145, 154, 156, 158
	Human	147, 149, 154, 160

EMPHASIS AREA	**KEY WORDS**	**PAGE**
Respiratory Diseases (Cond't)		
	In Vitro	139, 143, 147, 149, 153, 154
	In Vivo	139, 143, 152, 158
	Physical Agents	139, 143, 145, 149, 152, 153, 158, 160
Safety		
	Administrative Methods	165
	Engineering Controls Development	163
	Human	163
	Testing	165
Sidestream Smoking		---
Other Research for Occupational Safety and Health		
	Analytical Methods	179
	Animals	171, 174, 177, 184
	Cancer	186
	Engineering Controls Development	173, 176, 183
	Human	174, 181, 186

RESEARCH AND DEMONSTRATION GRANT SUMMARIES BY EMPHASIS AREA

Emphasis Areas

Asbestos and Asbestos Substitutes

Behavioral and Neurotoxic Effects

Cancer

Cardiovascular Diseases

Chronic Effects of Trauma

Control Technology

Dermatology

Digestive Diseases

Energy

Mining

Physical Agents

Protective Equipment

Radiation

Reproductive Effects

Respiratory Diseases

Safety

Sidestream Smoking

Other Research for Occupational Safety and Health

Other NIOSH Grant Programs

Demonstrations of Safe Asbestos Removal in Schools

Health Hazard Evaluation Cooperative Agreements

Surveillance Cooperative Agreements

☆U.S. GOVERNMENT PRINTING OFFICE: 1981--757-074/1066

blank page